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ROENTGENOGRAPHIC STUDIES OF THE EXCRETION OF DUSTS FROM THE LUNGS*

By A. E. BARCLAY, M.A., D.M., D.M.R.E.(Camb.), F.A.C.R., K. J. FRANKLIN, D.M., M.R.C.P., *and* R. G. MACBETH, B.M., M.A., F.R.C.S.(Ed.)

From the Nuffield Institute for Medical Research
OXFORD, ENGLAND

MANY workers have carried out dusting experiments with the object of discovering the changes produced by the dusts within the lung tissue. Our aim has been a different one. We have insufflated radiopaque dusts into the lungs of animals, in order to study the manner and rate of elimination of these dusts from the healthy respiratory tract. When we have satisfied ourselves on these points, we shall attempt to discover how, and perhaps also why, pathological processes can alter these two factors.

To the extent that we have employed radiopaque dusts to show up the bronchial tree, but not otherwise, our experiments have some correspondence with the clinical work of Chevalier Jackson, who from 1907 onwards used local depositions of such dusts to show the position of foreign bodies, etc., and who in 1918 made the first recorded insufflation into a human lung. He blew bismuth carbonate powder into the ascending branch of the left upper lobe bronchus for diagnostic purposes; no untoward symptoms resulted, and the bismuth disappeared completely from the lung within twenty-four hours. Chevalier Jackson was very pleased with the result of this daring experiment, and wrote: "The method opens up an enormous field for the investigation of the action of the living cilia in health and disease, the lymphatic drainage of the lung, the mapping out of bronchiectatic and abscess cavities, and so forth." Clerf's account of "bronchoscopic pneumonography," published in Jackson and Coates' book eleven years after the appearance of Jackson's paper, showed that the use of dust insufflations had by that date only fulfilled some of the original expectations, namely, those more specifically concerned with disease conditions. We know of no studies, corresponding with our animal ones, that have been made on healthy human beings. The technique of dust insufflation has, however, been overshadowed in recent years by that of intratracheal injection of iodized oil.

I. THE RADIOPAQUE DUSTS USED (FIG. 1)

1. *Bismuth carbonate.* This is a smooth, bland powder, the individual particles of which in our experiments varied from 3 to 12μ and were occasionally as large as 24μ (H. M. Carleton), but tended to agglomerate, especially in the presence of even a

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small amount of moisture. The pH of 1 gm. of the powder in 10 cc. glass-distilled water, as measured by means of the quinhydrone-veibel electrode, was 7.5 (Parke, Davis and Co.).

2. *Powdered lead glass.* To begin with, we ground up some of the glass ourselves in a mortar. In this way we obtained a good dusting powder with particles varying in size from 7 to 45μ, the majority being from 20 to 25μ (H. M. Carleton). Later, Parke, Davis and Co. produced for us a finer powder; they found that the particles of this averaged less than 5μ, and were remarkably uniform in size. This second powder, however, had two disadvantages. In the first place, it contained a certain amount of soluble lead; in the second place, it had a very low pH, namely 3.3, as compared with 9.1 for the glass we powdered ourselves (pH measured in similar fashion to that of bismuth carbonate above). The analysis of the lead glass, as given to us by the maker, was:

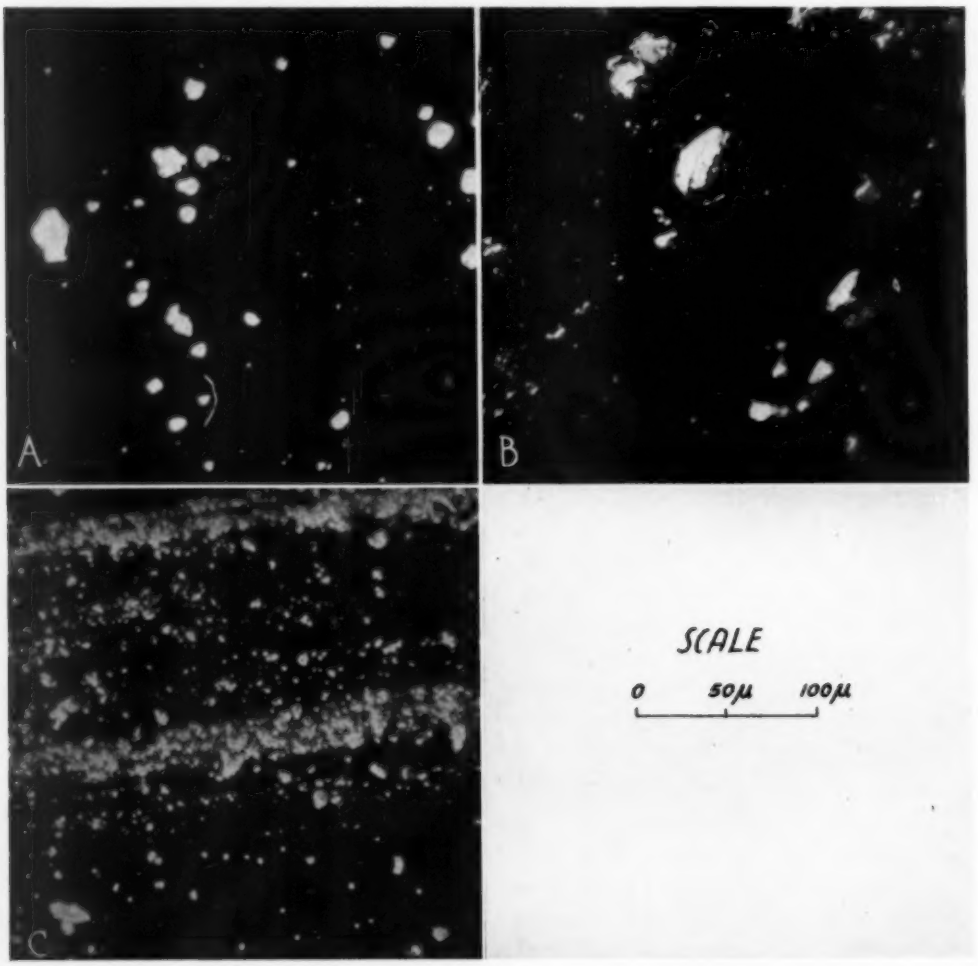

FIG. 1. Photomicrographs of dust particles, taken by Dr. H. M. Carleton. *A*, bismuth carbonate; *B*, lead glass No. 1; *C*, lead glass No. 2.

BaO	15.2		
PbO	47.5		
Sb_2O_3	0.7		
Al_2O_3	2.6		
Fe_2O_3	trace		
Na_2O	2.4		
SiO_2	31.8	Total	100.2

It is thus a silicate and in the proportions of its constituents, with the exception of lead and barium oxides, it resembles dust extracted from the lungs of some silicotic miners. An important difference between the particles of lead glass and those of bismuth salts is that the former are angular and hard, the latter amorphous and soft.

3. *Bismuth subnitrate*. This we tried, on the suggestion of Professor J. A. Gunn, in comparison with bismuth carbonate. The pH of the subnitrate, measured as above, was 3.3, i.e., it was definitely acid, whereas the carbonate was slightly alkaline. The particles measured from 6 to 12μ (H. M. Carleton).

II. OTHER SUBSTANCES INTRODUCED INTO THE LUNGS

1. *Acetic acid*, 1 in 20,000 in distilled water. The pH of this is 3.9 to 4.5 (J. St. L. Philpot). Negus (1934) stated that such a solution will completely arrest ciliary action, but presumably he was referring to experiments on isolated preparations.

2. *Syrup*, diluted with water, and with an admixture of lead glass powder.

3. *Normal saline*, after insufflations of dust.

III. THE ANIMALS USED

Cats were used throughout for the following reasons: They stand anesthetics better than most laboratory species. They have wide and distensible tracheae, so that dusting tubes can be introduced with ease and the outflow of air from the lungs is not entirely prevented when a tube is in place. Finally, their normal respiration rate approximates to the slow rate in man, which is a great advantage from the roentgenographic point of view. The disadvantages inherent in the use of cats are as follows: They will not breed readily in captivity, and for this and other reasons it is difficult to get a standard strain, as one can, for instance, with rabbits. Hence, each cat is a different individual, psychologically and otherwise, and comparisons must be made in the individual rather than between individuals. Further, even the individual varies from time to time, in our experience, in its activity. Rabbits might have been better subjects in some ways, but they are less tolerant of anesthetics, they have narrow and rather indistensible tracheae, and a high respiration rate.

IV. METHODS OF INSUFFLATING, ETC.

A preliminary roentgenogram was taken. Then, before being anesthetized, the subject was given, with aseptic precautions, an intramuscular injection of sterile atropine sulphate solution; the drug was administered in the dosage of 0.2 cc. of 1:10,000 solution per kg. body weight, i.e., slightly over human pre-anesthetic dosage. After an appropriate interval, castor oil was instilled into the conjunctival sacs, and the animal was anesthetized with 1:2 chloroform-ether mixture. Then, with the help of a child's laryngoscope of Jackson pattern, a sterile brass tube, 22 cm. long and with outside and inside diameters of 3 mm. and 1.5 mm. respectively, was introduced between the vocal cords into the trachea. In the earlier experiments the larynx was cocainized; later this procedure was discarded as unnecessary. While the animal was screened, the smooth, rounded end of the brass tube was pushed down the trachea until it was 1.0 to 1.5 cm. proximal to the bifurcation. In the early cases swabs were taken from this region, and these were found to be sterile. The practice was discontinued as there was evidence that the procedure damaged the cilia. A de Vilbiss insufflator, carrying the dust, was now connected by a short piece of rubber tubing to the brass tube, and the dust insufflated until it had reached an adequate concentration, and penetrated far enough, within the lungs, as observed by screening. (In all the later experiments, care was taken to insufflate synchronously with inspiration, and to allow as free air outflow as possible during the insufflations.) The tube was then withdrawn, and another roentgenogram taken; this was developed at once to check the observations made during the

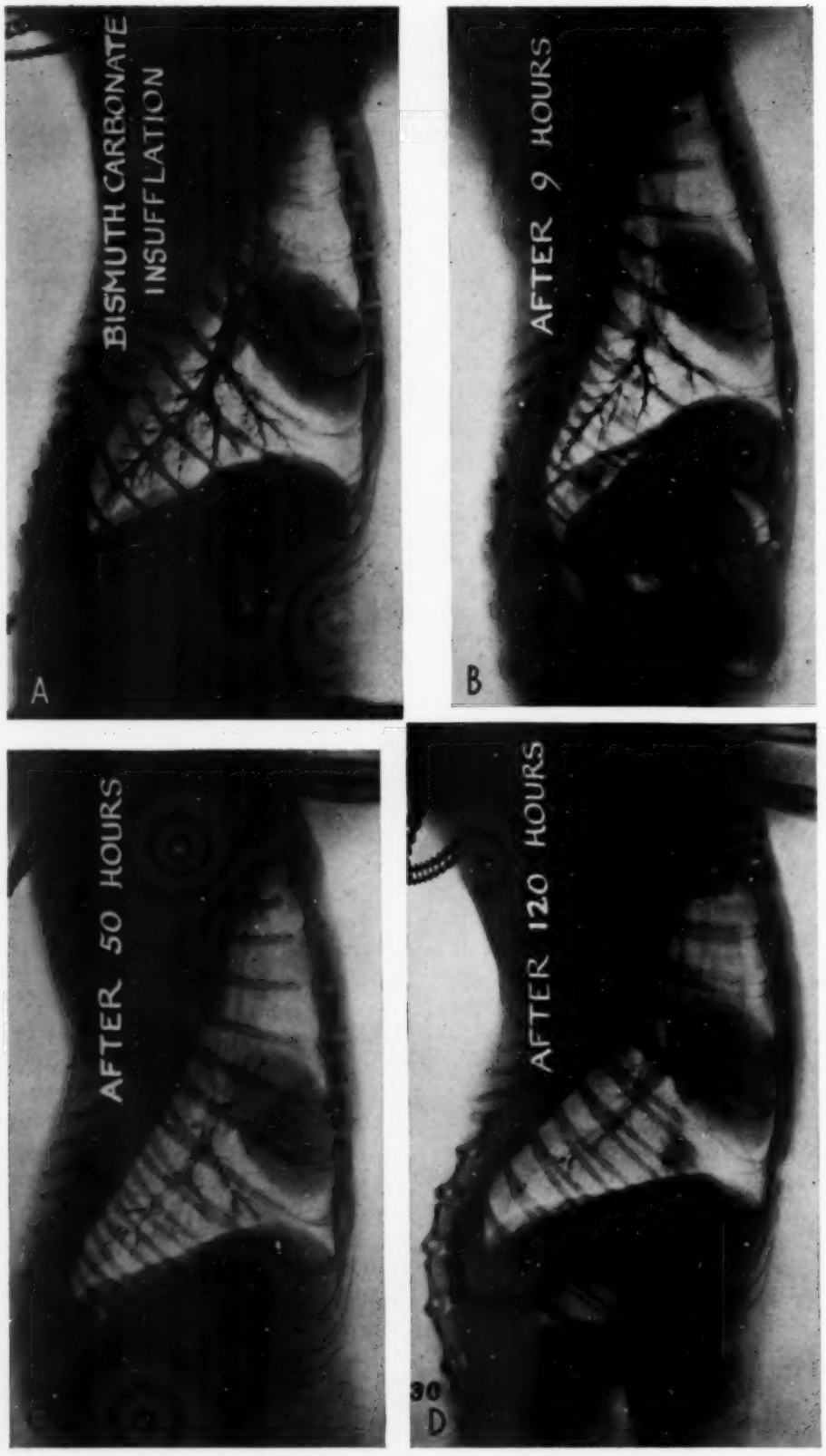

FIG. 2. Roentgenograms of a cat's lungs: *A*, immediately after insufflation of bismuth carbonate; *B*, nine hours; *C*, fifty hours, and *D*, 120 hours later. The lungs and trachea were quite clear of dust in 150 hours. Note in *B* the bismuth present in the alimentary tract after its excretion from the lungs.

screening. Finally, a second instillation of castor oil was made into the conjunctival sacs, and the animal was warmly wrapped up to await recovery from the anesthetic; this was, in most cases, very rapid. The volatile anesthetics were preferred to hypnotics, because of their rapid excretion, and also because the hypnotics, that on other counts would have been most suitable, depress the respiration and cause excessive salivation and bronchial secretion. Roentgenograms were taken at intervals until there was no evidence of the opaque dust to be seen in the lungs.

V. RESULTS

Preliminary Note. Substances insufflated, or introduced in other ways, into the lungs, invariably proceeded in greatest amount to the lower lobes; in no instance was the whole of the respiratory tissue affected, i.e., some always remained available for its normal function.

1. *Of dusting with bismuth carbonate.* Despite the tendency of the particles to agglomerate, the dust travelled well within the lungs; in most of the animals it penetrated into very fine bronchioles but never appeared to enter alveoli. Five cats were so dusted in our first series. They appeared perfectly normal in every respect after recovery from the anesthetic and suffered no detectable disability, pulmonary or otherwise. They did not cough and all the opaque dust was swallowed as it left the respiratory tract. The mass of the dust was excreted in from seven hours to three days, and the last traces had disappeared in from one to four days. Considering the amount of dust insufflated, we were amazed at the rapidity of its elimination. In all, we have now performed such dustings 14 times, with results that in general confirm the rates of excretion given above, though the maximum time was extended in one subject to 150 hours (Fig. 2). Second insufflations, carried out in some animals a short time after the first ones, have given very closely corresponding times, which suggests that the lungs suffered no damage from the experimental procedures.

2. *Of dusting with powdered lead glass.* In spite of the relatively large size of the particles, this was a good dusting agent; in most cases it outlined very fine bronchioles, but never, so far as we could judge, passed into alveoli. In our first series, it was tried on 4 subjects that had previously been insufflated with bismuth carbonate. These all returned the lead glass powder more rapidly than the bismuth salt, getting rid of the mass within a day and of the last trace within two days; a fifth cat, that had had no previous insufflation, was quite clear in seventeen hours (Fig. 3). The animals did not cough and were apparently in perfect health. Subsequent experiments have brought our total number of insufflations with this dust up to 15, but the picture given in respect of these first subjects remains materially unaltered, except for a single case, which may receive passing mention. In this one cat the mass of the dust took three days, and the last trace five days, to be eliminated. This delay was almost certainly due to over-inflation of the lungs during the insufflation, for, although the animal seemed quite well, a definite pneumothorax was visible on the roentgenogram; this result was therefore discarded as abnormal.

Insufflation of lead glass dust did not affect to any noticeable degree the excretory function of the lungs. Our records show that the dust was insufflated into 4 cats on more than one occasion, namely, into 2 of them three times and into the others twice; the intervals between the dustings varied from a week to a month, i.e., in some cases they were too brief for healing, had any serious damage been done. The times of excretion, nevertheless, were practically identical in all 10 observations; in only one was there a slight increase. In addition, the lungs showed no abnormality in any case after the dust had disappeared, and the animals were apparently perfectly well.

3. *Of the comparison of bismuth carbonate*

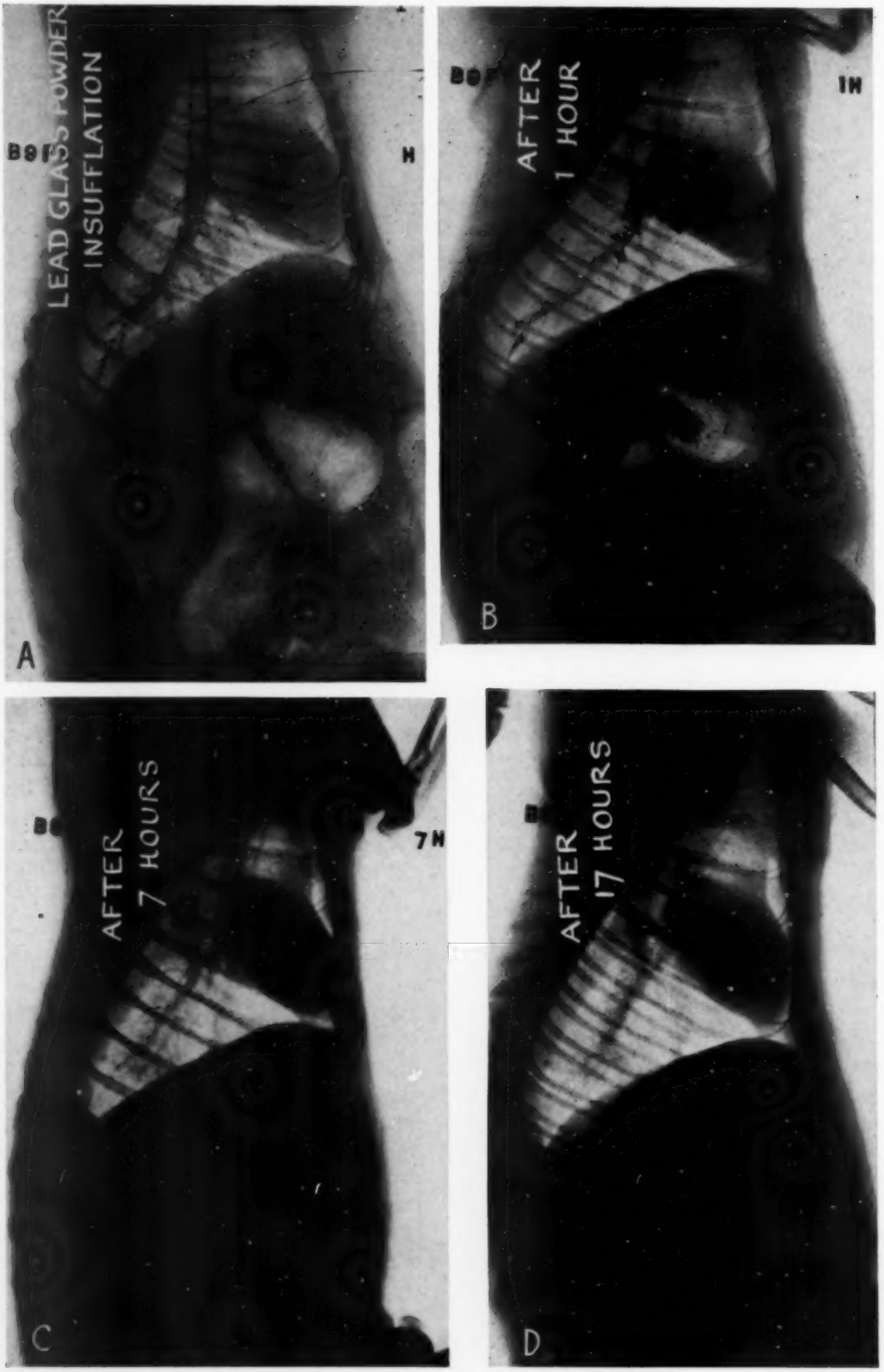

FIG. 3. Roentgenograms of a cat's lungs: *A*, immediately after insufflation of lead glass powder; *B*, one hour, *C*, seven hours, and *D*, seventeen hours later. There is still a trace of lead glass near the bifurcation of the trachea in *C* but none anywhere in *D*.

and bismuth subnitrate. The excretion times of the acid salt, bismuth subnitrate, tested six days after preliminary insufflations with the carbonate, were in 2 subjects the same as those found with the alkaline salt, in 2 other subjects less.

4. *Of previous introduction of 1:20,000 acetic acid*. Four cats were insufflated with bismuth carbonate and the excretion times determined. Some days later (five in the case of 2 of the cats, ten in the case of the others) 2 cc. of 1:20,000 acetic acid was slowly introduced into the trachea of each animal, which was then held up and rotated for some time in order that the acid should be widely distributed in the lungs. Six to fourteen minutes after the introduction of the acid, a fresh insufflation of bismuth carbonate was made. The excretion times were, if anything, shorter than in the control experiments. A point that arises from these experiments is that, apparently, the lungs had been able to absorb these relatively large quantities of fluid in the short intervals that elapsed before the insufflations. If it had not been so, it is probable that the fluid would have mixed with the dust and carried it into alveoli. This is in conformity with the roentgen observation of the rapidity with which we have observed the clearing up of lungs that have become water-logged through prolonged bronchoscopy during the extraction of foreign bodies.

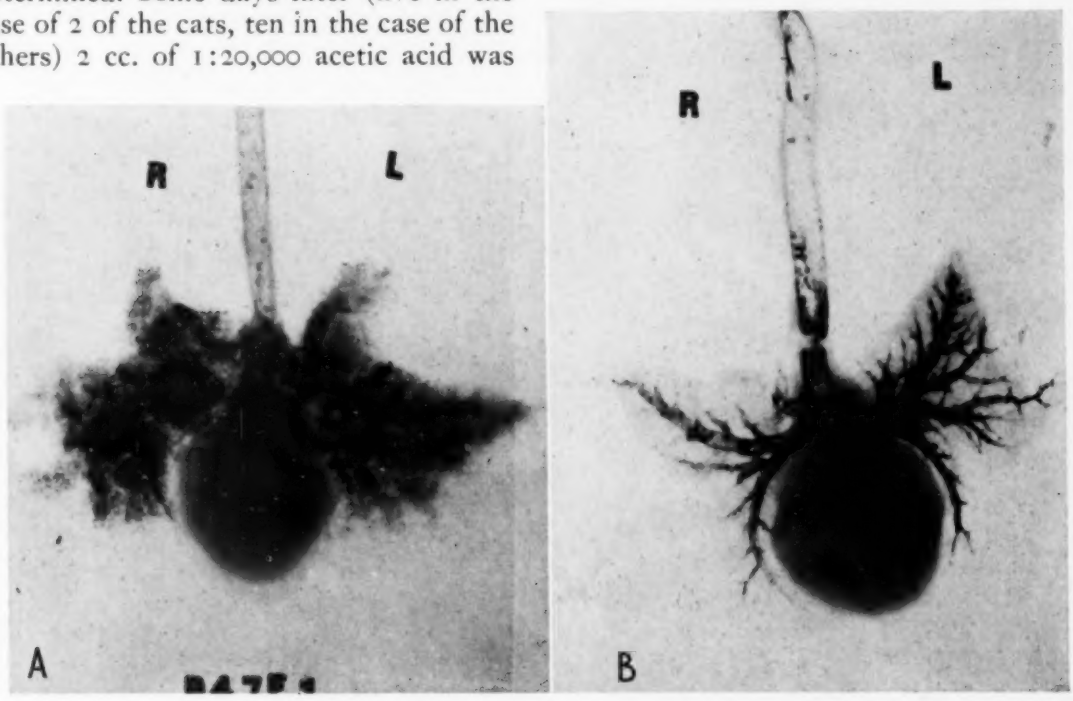

Fig. 4*A*. Roentgenogram of a cat's lungs, which were exsected very soon after the intratracheal introduction of a *liquid* mixture of lead glass powder and saline. The powder has passed into alveoli.

Fig. 4*B*. Roentgenogram of another cat's lungs, which were exsected very soon after an insufflation of the same lead glass powder in its *dry* state. The powder has not passed beyond the finest bronchioles.

5. *Of subsequent introduction of 1:20,000 acetic acid*. In 2 cats we reversed the above order of procedure, and followed insufflations of bismuth carbonate with introduction of acetic acid solution. In these cases the effects were quite different. The dust was carried by the fluid farther into the lungs, so that some soon reached alveoli and there gave a shadow for weeks. The animals, however, did not appear to suffer any inconvenience and they developed no cough.

6. *Of introduction of a mixture of lead*

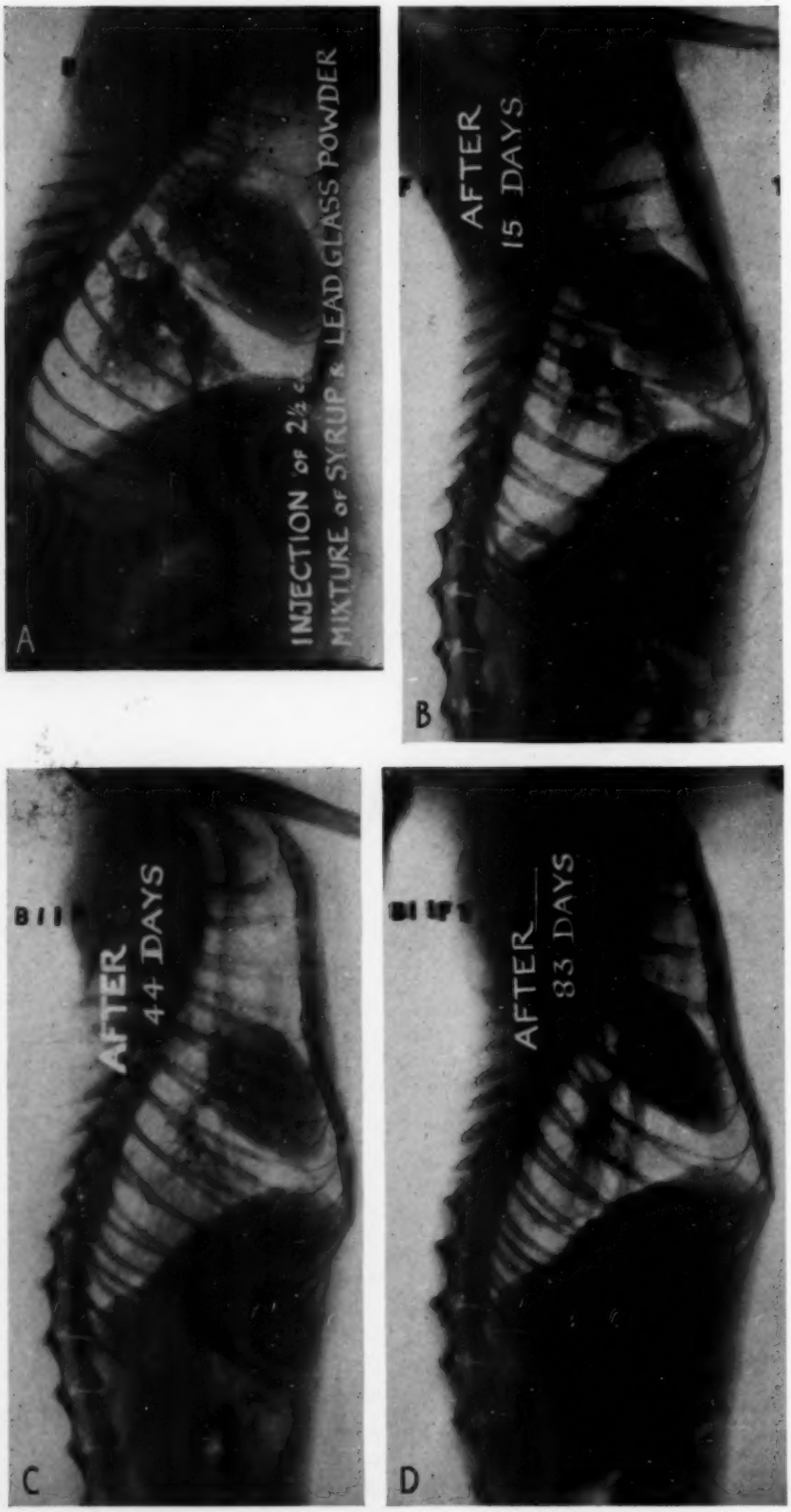

FIG. 5. Roentgenograms of the lungs of a cat, which had received an intratracheal injection of lead glass powder, suspended in dilute syrup. The injection passed into the left lung only. *A*, immediately after the injection. The dust is in alveoli and bronchi; from the latter it later disappeared within eight hours. *B*, fifteen days after the injection. There is still a fair amount of dust in the alveoli, though much has already been excreted from them. *C*, forty-four days after the injection. More dust has been excreted from the alveoli. *D*, eighty-three days after the injection. Still less dust is present in the alveoli.

glass dust and saline. Into the lungs of another cat was introduced 4.5 cc. of such a mixture. In a few minutes it had apparently reached alveoli; this assumption, which was based upon the roentgenological appearances, was confirmed by subsequent histological examination (H. M. Carleton). Figure 4*A* is a roentgenogram of the exsected lungs of this subject; it may be compared with Figure 4*B*, which is a similar roentgenogram of the lungs of a second cat, into which the same powder, *in its dry state*, had been introduced by insufflation.

7. *Of introduction of lead glass dust suspended in dilute syrup* (Figs. 5 and 6). In our early experiments, we wished to find a way of suppressing ciliary action for a time without causing any permanent damage to the epithelium. We conceived that a viscid substance like syrup would effect this; hence this particular experiment. The animal was in the left lateral position, so the suspension tracked down into the

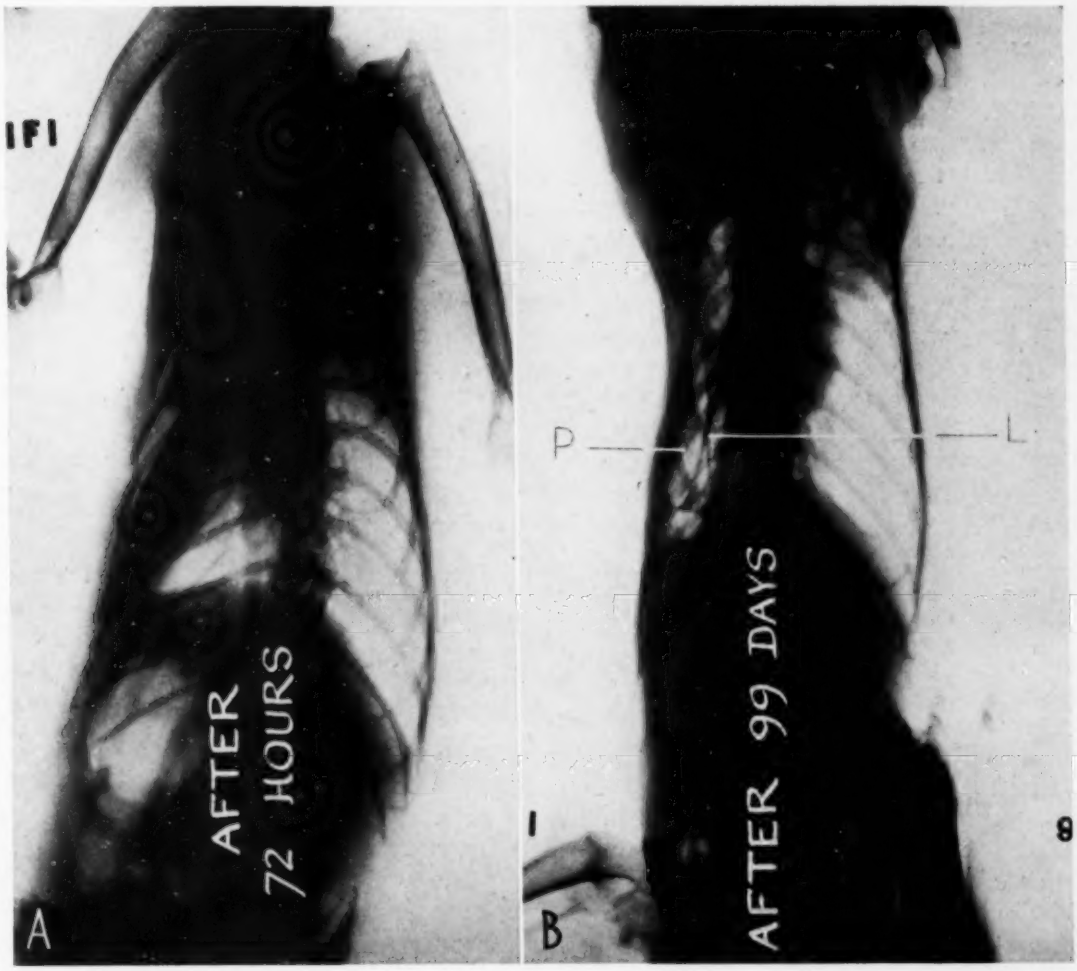

Fig. 6. Sagittal roentgenograms of the same cat as in Figure 5, to show the gradual shrinkage of the lung, into which the suspension was introduced. *A*, after seventy-two hours. The shadow of the dust is dispersed through the alveoli on the lateral surface of the lung; the two sides of the chest show no asymmetry. *B*, after ninety-nine days. There is a pneumothorax, *P*, presumably due to retraction of the affected lung, which is now a shrunken fibrotic mass. On its lateral surface is a narrow line, *L*, indicating the position of the remaining dust.

bronchi and bronchioles of the left lung only; soon, apparently, it was in alveoli. On the following day the shadow of the dust was distributed through the alveolar area on the surface of the lung, while the bronchioles and bronchi were practically clear. Excretion from the alveolar area proceeded extremely slowly, and some traces of the dust were still in it after three months. In the meantime, the lung had gradually become a shrunken and fibrosed mass, with little normal lung tissue remaining. The cat showed no signs, and remained as active as before, though it was appreciably thinner.

DISCUSSION

1. *The excretory mechanisms.* In any discussion of the excretory mechanisms of the lungs reference must be made to papers such as those of Gunn,[11] Proetz,[18] and Negus.[17] As a result of reading these and other communications, and of our own experience, we can affirm that the most important mechanism is that provided by the cilia and the secretion of mucus, for it extends over most of the respiratory tract, and is the only known means of clearing substances from this large area, except for the pathological (Negus) or psychopathological act of coughing. The ciliated epithelium is distributed through the trachea and bronchi down to very fine bronchioles, which are stated by Quain[19] to be of the order of 0.2 mm. in diameter. In human beings cilia are still present, according to Miller,[16] in bronchioles 0.35 mm. in diameter; they are not, on the other hand, seen in his figure of a bronchiole 0.25 mm. in diameter. Interspersed among the ciliated cells in tubes of this size are non-ciliated cells; in the larger tubes the ciliated cells are continuous, and even line the openings of the ducts. Proetz emphasized the importance of the mucous blanket, which forms a continuous layer over the ciliated epithelium, and is carried upwards, with the foreign bodies which are deposited on it, by the ciliary action. Much depends on the mucous blanket, for the ciliary action is rendered ineffective if it is either too scanty or too profuse, too dilute or too concentrated. Elsewhere (Barclay, Franklin and Macbeth;[4] Barclay and Franklin[2]) has been noted the tendency for the mucus to move spirally (clockwise, viewed from above) upwards, and the peculiar direction of movement at the areas of junction of bronchi. Indian ink, injected subpleurally into the lung of a decerebrate cat, takes only fourteen minutes to reach the distal end of the tracheal cannula, i.e., to travel about 4 cm. within the lung and 8 cm. up the trachea (Barclay and Franklin[2]). The rate of movement is considerably greater in the trachea than it is in the lung (Barclay and Franklin[2]), and a particle of fine starch powder may be carried along in the opened cat's trachea as fast as 3.5 cm. per minute (Florey, Carleton and Wells[8]). Negus (personal statement to R. G. M.) points out that cilia are not present on the vocal cords and anterior commissure of the larynx, but are present on the posterior commissure. Hence, all mucus must pass up by the posterior commissure, which partly explains why tuberculous lesions of the larynx are commonest in that region.

Inflammatory conditions may destroy ciliated epithelium, and it may not be regenerated; in such cases the mechanism of cough has to be brought into play (Negus) "In bronchitis, not only is there evidence of greatly increased production of mucus by the buried glands, but the ciliated surface epithelium itself may become almost totally replaced by cells of the goblet type" (Florey, Carleton and Wells[8]). Hence, any area that has been the scene of an inflammatory process may be vulnerable, for it may have lost the main weapon for combating and getting rid of foreign matter. Cummins,[7] however, states that even in the worst cases of pneumonoconiosis ciliated epithelium is usually retained to the end, despite the presence of pus in the bronchioles.

With regard to coughing, we may quote from Negus:[17] "Cough is connected with pathological" [and, we would add, psycho-

pathological] "processes and is not indulged in by healthy individuals, in whom ciliary activity provides the" [only] "important defensive mechanism." The receptor end-organs for the reflex are part of the vagus innervation of the respiratory and upper alimentary tracts, but the most sensitive ones are in the laryngeal region and at the bifurcation of the trachea, the former having the lower threshold; this is not only a clinical finding, but also our experimental one in animals just beginning to come out of deep anesthesia, while we were still insufflating. About the parts of the respiratory tract that are cleared by coughing there is less certainty; they will include these specially sensitive areas; they may also, perhaps, include the alveoli, but this is only hypothesis.

Coughing is not usually resorted to by healthy persons even in a dusty atmosphere but, in the presence of irritant fumes or smoke, it is the normal response to irritation of the mucous membrane. It is worthy of note that the people who live in the desert and spend most of their lives in the dust of camel trains or in archaeological diggings are said to be free from pulmonary disease and that coughing is rare—this we have on the authority of Sir Arnold Wilson, who has lived among the Arabs in the desert.

The mechanisms of excretion from the alveoli are not yet fully understood. Wandering phagocytic cells undoubtedly play an important part, particularly in the case of long-standing inhalations (see, for instance, Carleton[5]), but it is possible that other factors, e.g., the variation in volume of the alveoli with the phases of respiration, may come into the question.

The part played by the smooth muscle of the bronchi and (?) trachea in the process of excretion still needs further study. The muscle fibers are distributed in a "geodesic network" (Miller[16]), that must have a functional significance. In addition, Grancher[10] (1890) found that the muscle bands were relatively five times as thick in a bronchiole 1.0 mm. in diameter as they were in a bronchus 10.0 mm. in diameter, and other observers since then, e.g., Miller, have corroborated this finding that the tubes increase in muscularity as they decrease in caliber.

When, however, we pass from such anatomical findings to studies of the physiological actions of the smooth muscle, we come upon a conflict of views, which is in part due to the technical difficulties imposed by the rapid alternation of inspiration and expiration. Two examples will, perhaps, suffice to illustrate the divergence of opinion that obtains.

Hudson and Jarre[12] recalled that Chevalier Jackson had "repeatedly described a widening and contraction of the bronchi as seen through the bronchoscope." Such variation in caliber is clearly seen in Janker's roentgen cinematographic film of the cat's bronchial tree; there may be a 100 per cent increase in caliber, or 300 per cent increase in cross-section, of the bronchi during inspiration. Thornton's[20] recent work (1937) shows that the dilatation may be reflexly produced. On the other hand, mere widening and narrowing of the bronchial tubes is no evidence for an excretory action of the smooth muscle, which can only, one would imagine, be provided by peristalsis. Evidence for such peristaltic movement in human beings was furnished by Jarre, in cooperation with Hudson (Jarre[15]). By means of *direct* roentgen cinematography, they studied the bronchial movements during the excretion of injected lipiodol. "Peristaltic waves synchronized with the expiratory phase of respiration are found originating in the peripheral portions of the bronchial tree and progressing gradually towards the stem bronchi and trachea. These waves propel the liquid contents along their routes and evidently are able to empty the bronchial tree without invoking ciliary motion." On the other hand, Gordonoff,[9] working on animals with Janker's *indirect* roentgen cinematographic technique, found no evidence of peristaltic movement of the bronchial musculature.

If peristalsis of the bronchial muscula-

ture is analogous to peristalsis of the intestinal musculature (Barclay[1]), we should expect to find that it is largely a reserve mechanism, called upon, under appropriate conditions, to augment or replace the more normal propulsive forces. Such conditions, we think, may obtain after the injection of lipiodol, which can embarrass, or render inoperative, ciliary action.

2. *The amount of dust insufflated and the rate of its excretion.* We were unable to gauge the actual weight of dust which we insufflated into our cats, as we had to leave as free an exit as possible from the lungs, in order not to damage them from over-inflation, and hence a fair amount of the powder billowed out into the room. Nevertheless, we can safely say that inhaled dust could never attain even a very small fraction of the density of the radiopaque dusts that we insufflated into the lungs (Fig. 4*A*). The shortest time taken for excretion, seven hours, is in striking contrast with the quarter of an hour required for a subpleural injection of Indian ink (Barclay and Franklin[2]) but remarkably brief considering the size of the cilia, and the amount and density of the dust that their activity had to move. If such heavy dustings can be excreted in the times we have noted, *healthy* lungs should have no difficulty in coping with the minute amounts that are inhaled even in the most dusty atmospheres, provided the subject is given an adequate rest period away from these atmospheres. In no single instance in a total of 60 insufflations did the dust penetrate into alveoli. In 10 cases the dust extended to alveoli after some days, but in all of these there was bronchitis, bronchopneumonia, or other morbid condition. It is, perhaps, pertinent at this point to emphasize what has already been noted elsewhere (Barclay and Franklin[3]), namely, that a roentgenogram can show particles as small as 0.15 mm., provided there is sufficient contrast between the particle and its surroundings, as there was in our experiments.

3. *The effect of pH upon the excretion rate.* Our comparisons of the excretion times of bismuth subnitrate and carbonate, as also the effects of the introduction of acetic acid before insufflation, suggest that the lowering of pH has not that importance in the ciliated portion of the *intact animal's* respiratory tract which it has been shown to have in *isolated preparations*, that are no longer capable of continued existence. We have corroborative evidence of this from tissue culture experiments made by Dr. A. Burges, but it is to be published elsewhere at a later date. We may provisionally assume that acids, that are not strong and continuously produced, are rapidly rendered impotent by the mechanisms available for this purpose in the living animal. Alkaline substances may, perhaps, provide more difficulty, but the problem is one for the solution of which we require more experimental evidence than at present we possess.

4. *The effects of introduction of fluids.* The experiments with acetic acid solution introduced after dust insufflation, with the introduction of dust in dilute syrup and of dust in saline, show that the lungs have no mechanism to prevent such solutions from reaching the alveoli. Under such circumstances, excretion is very prolonged, and massive collapse of the lung may result, as in the "syrup cat." In this animal, it is worth noting, the pathological process continued steadily once it had begun, though the initiating agent was in large measure excreted long before we killed the animal to terminate the experiment. There was some histological evidence, in at least one of the animals, that cells were removing the dust and passing from the alveoli up the lymphatics; we never, however, saw any roentgenological evidence of lymph gland involvement.

The question of damp in the atmosphere is often raised. We have no information on the subject, but it seems possible that a moist atmosphere might tend to agglomerate particles of suitable dusts, and turn them into a semi-fluid, which could interfere with ciliary action.

SUMMARY

1. A roentgenographic technique is described for the determination of the excretion times of opaque dusts, insufflated into the lungs of cats.

2. When due precautions are taken, such insufflations do not cause damage to the lung tissue.

3. Insufflated dusts are not carried farther into the lungs than the distal termination of the ciliated epithelium, i.e., the defense against the penetration of dry dusts into the alveoli is extraordinarily efficient.

4. The dusts which we insufflated (bismuth carbonate and subnitrate, and lead glass powder) do not cause damage to the lungs.

5. Insufflated bismuth carbonate, which is neutral or slightly alkaline in reaction, is usually excreted in from one to four days. The subnitrate, which is strongly acid in reaction, is excreted, if anything, slightly more rapidly. Insufflated lead glass powder is usually excreted in from seven hours to two days.

6. The acidity or alkalinity of substances introduced into the lungs had no pronounced effect upon excretion times. This was in strong contrast with the results obtained by previous workers, who used isolated preparations of ciliated epithelium.

7. Dusts mixed with various fluids, and introduced into the trachea, were not arrested by the ciliated epithelium but passed into alveoli, from which they were slowly excreted over periods of weeks. There does not appear to be any defense mechanism to prevent fluids from entering the alveoli. There was no roentgenological evidence that the dusts in these fluids passed to the lymph nodes during their excretion, though particles as small as 0.15 mm. are detectable in roentgenograms, if the contrast is adequate, as it was shown to be in our experiments.

8. We consider that the technique is sufficient to give a standard, by which one may gauge the delay produced by pathological processes occurring within the lungs.

We have, then, more or less unwittingly, done something to fill up the gaps in Chevalier Jackson's scheme, for we have studied the end-results of ciliary activity, and we have some negative reports on the question of lymphatic drainage. In addition, by our studies of the behavior of radiopaque fluid mixtures, introduced into the lungs, we have shown that there is much to be said for the older technique of dust insufflation, as opposed to that of injection of iodized oil. Indeed, we have already been approached at the time of writing this (June 7, 1937) in connection with the clinical possibilities of the former method. The only possible danger seems to be that of an undue absorption of bismuth from large areas, denuded by morbid processes of their ciliated epithelium; in the healthy lung the dust would be removed too rapidly by the normal escalator mechanism that is provided by the mucous blanket and its motive force, ciliary action.

We wish to thank the Director of the Institute, Professor J. A. Gunn, for his interest and suggestions, Dr. H. M. Carleton for his histological reports and very valuable criticism, and Mr. J. St. L. Philpot for one pH determination. For the other pH values, as also for the preparation of the second lead glass dust, we are indebted to Parke, Davis and Co. For the systematic recording and classification of the data we obtained our best thanks go to Miss M. M. L. Prichard. We also wish to thank Miss C. J. Gibson for help of various kinds. Finally, we wish to acknowledge the expert assistance given by Mr. Maurice Tuckey, technician to the Institute, during the experimental and photographic procedures.

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MEDIASTINAL HERNIA IN THE ABSENCE OF PNEUMOTHORAX*

By HERBERT C. MAIER, M.D., Med.Sc.D.
University of Michigan Hospital
ANN ARBOR, MICHIGAN

MEDIASTINAL hernia is the protrusion of a portion of the contents of the pleural space of one hemithorax with evagination of the mediastinal pleura through the mediastinal partition into the contralateral hemithorax. This is not rare during the administration of therapeutic pneumothorax, and is particularly likely to occur if positive pressures are used, although it may appear with negative pressures. Herniation may develop, however, as a result of pathological processes within the thorax in the absence of pneumothorax or previous operative procedure. This has not been generally recognized. In this article discussion will be limited to mediastinal herniation in cases without pneumothorax because the subject of mediastinal hernia with pneumothorax has been well presented by Packard,[9] Doub and Jones,[5] and others.

The recognition of a mediastinal hernia in the absence of a pneumothorax is of definite clinical importance. During an attempted therapeutic pneumothorax in such a case a contralateral pneumothorax may result. If such mediastinal hernia has not been recognized prior to an intrathoracic surgical procedure, such as a pneumonectomy, the opposite pleural cavity may be opened inadvertently, and a contralateral pneumothorax produced. Occasionally, the herniated normal lung may underlie a portion of the ribs resected during a thoracoplasty, which will afford a possibility of injury to the pleura of the opposite side. If the operator should be unaware of a mediastinal herniation caused by an empyema, serious complications may follow the inadvertent surgical exposure of the opposite uninfected pleural space.

Mediastinal herniation should not be confused with the deviation of the mediastinum common in thoracic disease. Some mediastinal displacement is usually associated with the herniation, but in mediastinal hernia a portion of the mediastinal pleura of one side has penetrated through the mediastinum and invaginated a portion of the opposite pleural cavity.

ANATOMY

In man, the various structures throughout most of the mediastinum form a rather effective barrier between the two pleural cavities. There are three "weak places," however, in which only loose connective tissue separates the parietal pleurae of the two sides. Mediastinal herniae have been observed in each of these weak places.

One such area lies immediately behind the sternum in the anterior portion of the mediastinum where the medial reflections of the parietal pleurae are normally very close together. The majority of essayists consider this to extend from the first to the third ribs anteriorly. However, Packard[9] cited 4 cases of mediastinal herniation associated with pneumothorax in which the bulge extended from the first to the fifth ribs anteriorly. In one of our cases (Case IV) an anterior hernia extended down almost to the diaphragm.

Another weak place is in the lower posterior mediastinum between the aorta posteriorly and the esophagus anteriorly from the level of the fifth to the eleventh thoracic vertebrae. Herniation occurs much less frequently through this area than in the upper anterior mediastinum, and the latter herniae tend to be larger. It is stated in the literature that a posterior mediastinal hernia practically always extends from right to left, and not in the opposite direction. According to Nitsch,[8] such herniae may bulge from right to left between the aorta and the esophagus, but when pressure is brought to

* From the Department of Surgery, University of Michigan. Aided by the James and Elizabeth Inglis Fund for Thoracic Surgery.

bear on these structures from the left pleural cavity, the esophagus overlaps the aorta and thereby makes a barrier to the protrusion.

There is a third mediastinal weak place in the upper posterior portion of the mediastinum where the pleurae of the two hemithoraces are separated only by a very small amount of connective tissue. This area lies between the vertebrae posteriorly and the esophagus anteriorly from the level of the third to the fifth thoracic vertebrae. This upper posterior weak place is separated from the lower posterior one by the vena azygos. A discussion of the roentgenologic appearance of this upper posterior mediastinal region and its significance in roentgenological diagnosis has been presented by Bársony and Wald.[1] Mediastinal herniation at this site is rare (Fig. 3).

ETIOLOGY AND PATHOLOGY

Any pathologic process which tends to cause an appreciable difference between the intrapleural pressure of the opposing hemithoraces may result in a mediastinal hernia. The effect which prior or present disease processes have had upon the tissue of the mediastinum and the mediastinal pleura is an important factor in determining whether mediastinal herniation is likely to occur. If much fibrosis or infiltration of the mediastinum has occurred, the chances of herniation are diminished because greater intrapleural pressure changes would then be necessary to produce bulging of the mediastinal pleura. Mediastinal herniation in the absence of pneumothorax is usually seen in conditions in which the pressure difference in the two pleural cavities has existed for a considerable period of time. This is because there is a gradual stretching of the mediastinal pleura in these instances.

Mediastinal herniae may be divided into two groups. In one group the protrusion is toward the normal or less involved side, as in certain cases of massive or encapsulated empyemas, and in pneumothorax. In this group the disease process or pneumothorax has caused an elevation in intrapleural pressure of sufficient degree to produce bulging of the mediastinal pleura into the opposite side. For this reason these have been called pulsion herniae by some authors.

In the other group there is an invagination of the diseased side by the compensatorily enlarged contralateral lung. In such cases there is usually a deflation or fibrosis of a considerable portion of one lung so that it occupies a smaller space than normally. This results in a more negative intrapleural pressure on the diseased side and may result in a bulging of the opposite lung through the mediastinum into this side. Here one is dealing with an adjustive mechanism of the same type as that described by Rienhoff[10] after pneumonectomy and post-traumatic atrophy of the lung. The normal lung undergoes compensatory enlargement and fills a part of the space originally occupied by the diseased lung. Included in this second group of mediastinal herniae are those cases in which pulmonary expansion is for various reasons incomplete after the abandonment of a pneumothorax. Also, contracting fibrous tissue associated with an adhesive pleuritis may exert a pull on a portion of the mediastinal pleura and produce herniation. Stéphani and Kirsch[12] believed traction of the diseased lung to be the cause of small mediastinal herniae unassociated with pneumothorax. Dahm[3] has described mediastinal "traction bands" which he thought were produced by a pull on the mediastinal pleura; these may simulate mediastinal herniae.

The condition which most commonly produces mediastinal herniation is pulmonary tuberculosis. This is due to the fact that both extensive atelectasis and fibrosis are frequently present in this disease. It has been observed that the atelectasis discovered in many tuberculous individuals is due to a tuberculous tracheobronchitis with a variable degree of bronchial stenosis.[11] In those patients who have undergone previous pneumothorax therapy it is not possible to say definitely what rôle the abandoned pneumothorax played in the production of the mediastinal hernia. It is quite probable, however, that the pleuritis associated with

the pneumothorax, and the greater discrepancy in the intrapleural pressures of the hemithoraces during the period of pulmonary expansion are important factors in an invagination by the mediastinal pleura from the opposing side. The majority of the patients having mediastinal hernia in the absence of pneumothorax who have been observed in this clinic have had pulmonary tuberculosis. Most of these patients had tuberculous involvement of the bronchi.

Other causes of mediastinal herniation are bronchial tumors producing atelectasis; extensive unilateral suppurative bronchiectasis with much fibrosis and pulmonary contraction (Case I); cystic disease of one lung; and atelectasis following aspiration of a foreign body (Case VII), or following other forms of bronchial occlusion.

Mediastinal herniation may also occur in cases of empyema.[2,7] If there is a bronchopleural fistula associated with the empyema, there may be greater likelihood of the development of increased pressure within the empyema cavity, and therefore a mediastinal hernia is more likely to result. A small posterior mediastinal hernia in addition to gross mediastinal displacement may account in some instances for the presence of Grocco's sign (a paravertebral triangular area of dullness at the base of the uninvolved side) in cases of empyema.

The extreme degree to which the protrusion of the diseased pleura into the opposite side may progress is demonstrated by an unusual case reported by Eggers.[6] His patient apparently had had for two years a pyopneumothorax secondary to a pulmonary abscess. Roentgenograms showed a single fluid level which extended virtually across the entire chest with a resultant appearance of a bilateral empyema. At operation the empyema cavity was carefully examined, and was found to protrude across the middle of the chest in front of the heart into the opposite hemithoracic space. Further films with the injection of opaque substance into the empyema cavity about nine weeks after open drainage of the empyema showed that the extension to the opposite side had disappeared. At no time was there evidence of involvement of the opposite pleural space.

DIAGNOSIS

The possibility of the existence of a mediastinal hernia should be borne in mind in any patient with thoracic disease possibly affecting a change in the position of the mediastinum. In cases of pulmonary tuberculosis with atelectasis of a large portion of one lung for a considerable time, mediastinal hernia is especially prone to occur. This is especially true if the patient has been at some time treated with pneumothorax, and if markedly negative intrapleural pressures had developed when the pneumothorax was abandoned. The same is true in any patient with atelectasis or fibrosis of one lung due to other causes.

There are no physical signs which are pathognomonic of mediastinal herniation. The physical signs which are present are often interpreted in another way. For example, if a large anterior mediastinal hernia is present in a case of extensive atelectasis of one lung, the relatively normal resonance and breath sounds which may be found in the upper anterior chest on the diseased side may be interpreted as an uninvolved portion of the lung on the affected side rather than a herniation of the opposite lung.

It is questionable whether there are any definite symptoms attributable to mediastinal herniation in the absence of pneumothorax. Although there may be dyspnea, palpitation, and signs of cardiorespiratory embarrassment in patients with mediastinal hernia due to pneumothorax, no similar symptoms or signs which could be definitely and solely attributed to the herniation itself have been encountered in the group of cases reported in this article, when not associated with pneumothorax. There may, however, be symptoms due to the mediastinal displacement which accompanies the herniation.

The diagnosis of mediastinal hernia rests almost entirely upon roentgenologic findings. If only the routine type of chest films

are made, the presence of herniation will often be overlooked. This is because most of the cases of mediastinal hernia unassociated with pneumothorax are due to atelectasis or fibrosis of one lung. As a result there is considerable increase in density on the affected side, and if some aerated lung from the opposite hemithorax has herniated through the mediastinum, it will not necessarily be evident through this dense shadow. Stereoscopic roentgenograms with the Potter-Bucky diaphragm are a great aid in the diagnosis of such herniae. In this type of roentgenogram there is sufficient contrast between the diseased lung and the aerated lung to permit a clear differentiation in most cases. The border of the bulging lung appears as a well-defined curved line which extends out from the mediastinal shadow. In cases of anterior herniation the upper border can be traced across the mediastinum at the level of the sternoclavicular joint. The level of the lower limit of the hernia varies with the size of the hernia; in large herniae it extends almost to the diaphragm. An upper posterior hernia can be differentiated from an anterior hernia because the former is for the most part above the sternoclavicular level (Fig. 3). A lower posterior hernia has its upper margin some distance below the clavicles (Fig. 5). In the types of cases reported in this paper, the hernial bulge has its convexity toward the diseased side and is superimposed on the usually more dense shadow of the diseased lung. With stereoscopic films the anterior position of an anterior mediastinal hernia or the posterior position of a posterior mediastinal hernia can usually be determined as confirmatory evidence of the diagnosis. A lateral projection is an aid in diagnosis, particularly of an anterior hernia, as is shown in Case IV (Fig. 4). This lateral film shows a deep retrosternal space with hyperaerated lung in front of the large vessels, and if the hernia is large, also in front of the heart.

Many mediastinal herniae in cases of pneumothorax are not seen on routine chest roentgenograms because these films are taken at the end of a deep inspiration and the hernia may be present only during expiration, or at least is more clearly visible during expiration. In cases of mediastinal hernia without pneumothorax, however, the hernia is larger during inspiration. These herniae are to be seen best, therefore, on films exposed at the height of inspiration. The variations with respiration may be seen in one of our cases (Fig. 7). Roentgenoscopic and kymographic studies also demonstrate well the fluctuation in size of the hernia with respiratory movement.

Bronchography may be an aid in the diagnosis of mediastinal herniation. When iodized oil is introduced into the bronchi of a lung which has herniated, the protrusion of part of that lung through the mediastinum can be demonstrated. This is well illustrated in Case I (Fig. 1). In this same case the bronchogram of the diseased shrunken lung also aids in the diagnosis of the anterior mediastinal hernia because it shows the downward and backward displacement of the bronchial tree of the upper lobe of the bronchiectatic lung associated with the large amount of the contralateral lung which has herniated through the upper anterior mediastinum.

It is important to differentiate between mediastinal displacement and mediastinal herniation. In the upper mediastinum the relation of the pulmonary border to the trachea can usually be seen in studies made using the Potter-Bucky diaphragm. Unless the lung protrudes beyond the trachea into the opposite side, the condition should not be called a mediastinal hernia.

Bronchoscopy may give additional corroborative evidence in the diagnosis of mediastinal herniation. In cases of large anterior mediastinal herniae the carina is usually rotated. The orifice of the upper lobe bronchus on the invaginated side may have a more posterior position. Contralaterally the orifice of the upper lobe bronchus has a more anterior position than usual. These bronchoscopic findings are the result of the rotation which the herniating lung has undergone as its anteromedial border extends farther toward the opposite side.

TREATMENT

In cases of mediastinal hernia in the absence of pneumothorax the herniation itself requires no treatment. It is an adjustive mechanism of the same type as is seen after the surgical removal of one lung. Treatment of the diseased lung, however, will often be necessary. The symptoms of dyspnea and tachycardia which some of these patients have may be relieved after a thoracoplasty or other procedure has been performed on the diseased side. How much of this relief of symptoms is due to diminution of the mediastinal deviation and how much to the effect of the operative procedure on the mediastinal herniation or torsion of the tracheobronchial tree, it is difficult to say. It seems likely that most of the symptoms are due to the torsion and deviation of the mediastinum rather than the mediastinal herniation.

CLINICAL SIGNIFICANCE

A mediastinal hernia may be confused with a pulmonary cavity on a roentgenogram. In empyemas which protrude through the mediastinum, the appearance may simulate that of a mediastinal abscess or even a bilateral empyema. In cases of pulmonary tuberculosis treated by thoracoplasty, herniated normal lung might be interpreted as being inadequately collapsed diseased lung on the thoracoplasty side (Fig. 5).

Another reason for the importance of the recognition of mediastinal hernia lies in the avoidance of injury to the opposite pleural cavity during operation, thoracentesis, and during induction of artificial pneumothorax anteriorly. Hence, the possibility of such a hernia must be remembered in the interpretation of roentgenologic shadows.

Over 30 cases of mediastinal hernia in the absence of pneumothorax have been observed in this clinic. Included in this report are 7 illustrative cases.

ILLUSTRATIVE CASES

Case 1. J. S. (No. 381011), male, aged twenty-three, was admitted May 1, 1936. He had had a severe cough productive of much purulent sputum for nine years. Seven years ago the patient was treated with a left pneumothorax for a three months' period, but the lung was then allowed to re-expand. Physical examination revealed considerable deviation of the trachea to the left. The left hemithorax was smaller than the right, and respiratory motion was less on the left. There was dullness over the lower two-thirds of the left chest, and coarse râles were present. The heart was displaced to the left.

Bronchoscopy showed displacement of the carina toward the left side and some rotation in a counterclockwise direction. The left upper lobe bronchus seemed to extend from the main bronchus in a descending manner which permitted one to visualize its lumen for a considerable distance. The right upper lobe orifice was almost directly anterior.

Roentgenograms of the chest showed a shift of the heart and mediastinum to the left. The right pulmonary field was clear. On the left the diaphragm was sharply elevated. The upper portion of the left hemithorax was clear. In the lower third of the left pulmonary field there was infiltration with evidence of multiple cavity formation.

A left bronchogram showed very extensive gross saccular bronchiectasis of most of the left lung. The upper lobe bronchus had assumed a more downward course than is normal.

A right bronchogram showed some branches of the right upper lobe bronchus, all of the middle lobe bronchus, and the ventral basilar ramus of the lower lobe bronchus extending well over into the left hemithorax (Fig. 1). This definitely demonstrated the presence of a large anterior mediastinal herniation from the right with some rotation of the mediastinum. The evidence indicated an extensive diminution in volume of the left lung with displacement of the heart and mediastinum to the left and posteriorly, and a compensatory enlargement and rotation of the right lung, predominantly of the right upper and middle lobes, with the latter extending almost to the left midclavicular line.

A left total pneumonectomy was done by Dr. Cameron Haight. At operation the upper anterior portion of the left hemithorax was occupied by the right lung. Great care was taken so as not to open the right pleural cavity. A large anterior lappet of the right lung could be clearly seen through the hernial wall. The lung bulged into the left chest even when no positive pressure anesthesia was being em-

ployed. The left lung was small, fibrotic, and densely adherent.

Comment. In this case the left lung had undergone fibrosis due to long-standing suppuration. The patient had been treated with pneumothorax for a short time. These two factors had led to mediastinal herniation. The location of the bronchial orifices as seen on bronchoscopy, and the direction of the bronchi of the right lung as seen in the bronchogram, confirm the fact that the right lung had undergone rotation and had herniated through the mediastinum. The clear pulmonary field visualized in the left upper chest on the roentgenograms was actually chiefly herniated right lung (as confirmed at operation).

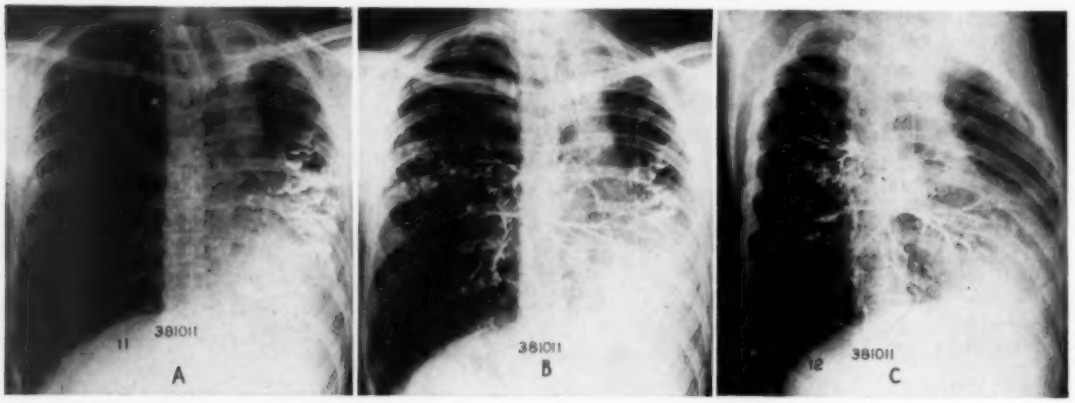

FIG. 1. Case I. *A*, left bronchogram showing saccular bronchiectasis of entire left lung. The diseased lung shows considerable diminution in volume. *B*, bronchogram showing branches of the right middle and lower lobe bronchi extending far into the left hemithorax superimposed on the residuum of the left bronchogram. *C*, right anterior oblique film demonstrating the extensive compensatory enlargement of the right lung involving chiefly the ventral portion of the upper lobe and of the middle lobe as indicated by their oil-filled bronchi.

CASE II. L. C. (No. 380106), female, aged thirty-two, was admitted April 16, 1936. In 1930 she had developed a productive cough, fever, general malaise, fatigue, night sweats and loss of weight. Roentgenograms at that time showed pulmonary tuberculosis. She had many episodes characterized by pain in the left chest, high fever, malaise and non-productive cough, followed by the sudden raising of a large amount of sputum and the subsidence of fever and malaise. In 1931 a left pneumothorax was instituted. In 1932 the pneumothorax refills were discontinued, but the lung remained collapsed and a high negative pressure developed. A left permanent phrenic nerve interruption was done in 1932. The febrile episodes increased in frequency.

Physical examination revealed that the trachea was deviated to the left. There were dullness and diminished breath sounds over the entire left chest. The heart was displaced to the left.

Bronchoscopy revealed the carina to be deviated to the left. There was almost complete stenosis of the left main bronchus.

Frontal stereoscopic roentgenograms showed the heart and mediastinum shifted into the left hemithorax. The trachea was deviated rather sharply to the left. On the routine film the left hemithorax was obscured by a homogeneous density. In the films made with the Potter-Bucky diaphragm, mediastinal herniation could be seen beginning at about the level of the middle of the manubrium sterni, extending laterally almost to the left axilla, downward beneath the second and third ribs, and returning to the midline opposite the level of the fifth cartilage (Fig. 2). Lateral projection with the Potter-Bucky diaphragm showed definite deepening of the anterior mediastinal space, with herniation of the lung anteriorly.

As the patient was progressing unfavorably after a long period of conservative treatment, and as attempted dilatation of the almost completely stenosed left bronchus was unsuccessful, pneumonectomy was done by Dr. John Alexander. The entire lung was densely adherent

everywhere. The right lung was seen to bulge toward the left side through the anterior mediastinal weak place. The entire mediastinum was also displaced somewhat toward the left. The left lung was less than half the normal size.

Comment. This patient had repeated episodes of atelectasis of the entire right lung secondary to bronchial stenosis over a six-year period. Due to atelectasis the lung could not re-expand when pneumothorax was discontinued. These factors undoubtedly led to the mediastinal herniation. The mediastinal hernia, which was diagnosed on the roentgenograms, was confirmed at operation.

Case III. F. E. (No. 366099), female, aged twenty-seven, was admitted August 8, 1935. She had had pulmonary tuberculosis for six years. The disease began with a left-sided pleurisy. Induced pneumothorax was attempted on the left side but was unsuccessful. Examination revealed tracheal deviation to the left. There were diminished expansion, dullness and diminished breath sounds over the left chest.

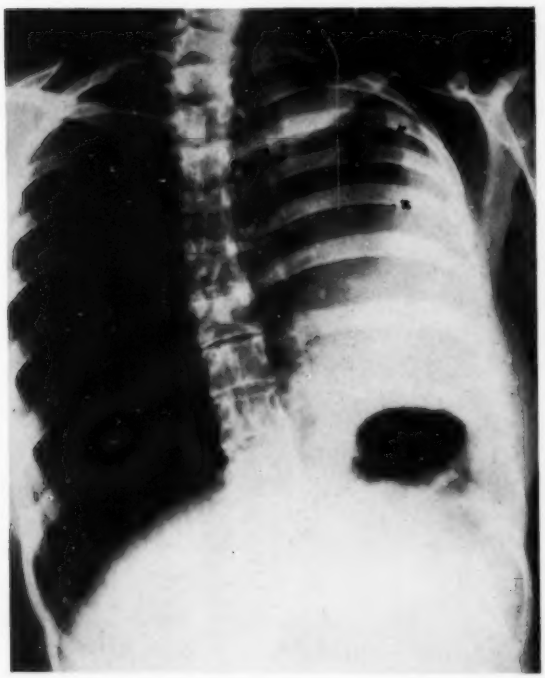

Fig. 2. Case II. Border of large anterior mediastinal hernia from right indicated by arrows. Atelectasis of left lung.

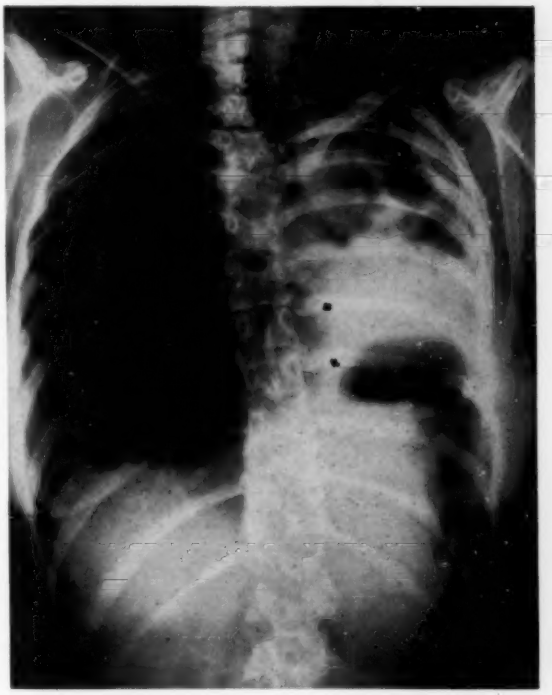

Fig. 3. Case III. Upper pair of arrows indicates border of right lung which has herniated through the upper posterior mediastinal weak place. Lower pair of arrows indicates lower posterior mediastinal hernia. Far advanced tuberculosis of left lung.

Bronchoscopy showed tuberculous involvement of the left bronchus without stenosis.

Routine frontal stereoscopic films of the thorax showed displacement of the heart and mediastinum to the left. There was gross excavation in portions of the left pulmonary field, and there was dense pleural thickening. Studies with the Potter-Bucky diaphragm demonstrated herniation of the right lung in the lower posterior mediastinum. There was also a small hernia in the upper posterior mediastinal weak place (Fig. 3). The anterior mediastinal hernia, which was also present, could not be seen on most of the posteroanterior films.

A left extrapleural thoracoplasty was done. On several occasions during the postoperative period the patient had paroxysmal tachycardia which she had apparently also had on one occasion a few months before admission to the hospital. No definite roentgenological evidence of residual lower posterior mediastinal herniation was to be seen after completion of the thoracoplasty. A small anterior and upper posterior mediastinal herniation remained.

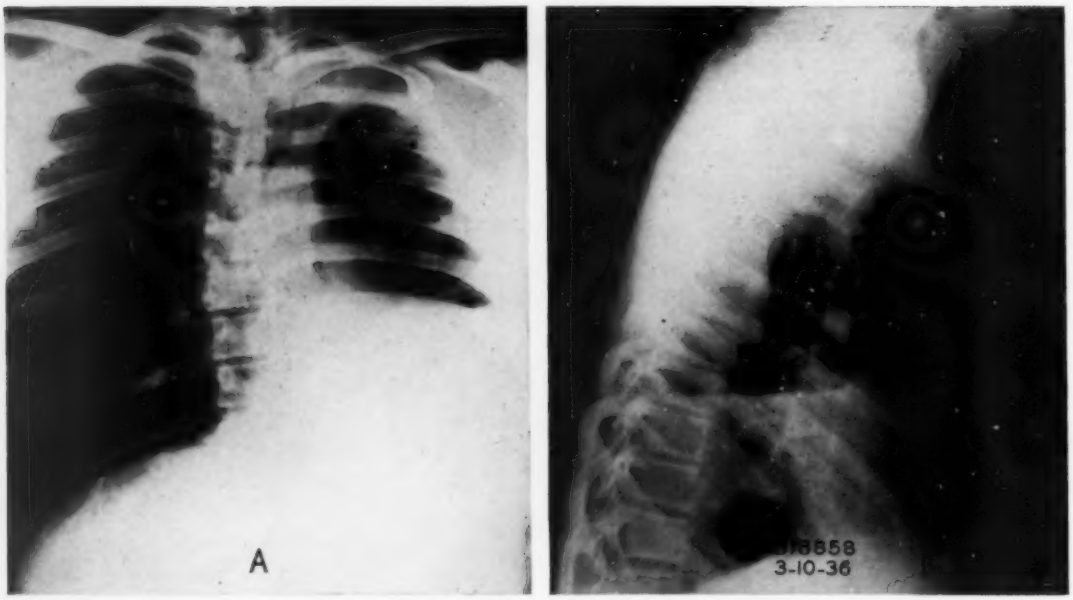

Fig. 4. Case iv. *A*, arrows indicate border of right lung which has herniated through the anterior mediastinum overlying the huge intrapulmonary tuberculous cavity in left lung. *B*, lateral film showing large anterior mediastinal hernia extending retrosternally downward almost to the diaphragm.

Comment. This patient had mediastinal herniation although she had never had any pneumothorax. The attacks of paroxysmal tachycardia may have been related to the mediastinal displacement and mediastinal herniation. This case is an example of the rare upper posterior mediastinal hernia.

Case iv. A. D. (No. 375858), male, aged twenty-seven, was admitted February 20, 1936. His illness began in 1929 with a left pleural effusion. During the following years the patient complained of weakness, productive cough, and weight loss. During the past two years he had had attacks of dyspnea which at times were quite severe. Productive cough continued and sputum was persistently positive for tubercle bacilli.

Physical examination revealed a slight lag in respiration on the left side. There were dullness and râles over the entire left lung. Breath sounds were bronchial in character in the left axillary region. The heart was displaced to the left.

Bronchoscopy showed a fibrostenotic, nonulcerative, tuberculous bronchitis of the left bronchus.

Roentgenograms of the chest showed the heart and mediastinum shifted to the left. On the left there was a huge space occupied chiefly by air with a small amount of fluid in the lower portion of the space. This was thought to be either a huge intrapulmonary cavity or a pyopneumothorax. Films with the Potter-Bucky diaphragm showed gross herniation of the right lung across the anterior mediastinal area (Fig. 4). There was also partial herniation of the right lung through the posterior inferior mediastinal weak place seen on some of the films. Lateral roentgenograms using the Potter-Bucky diaphragm showed the large anterior mediastinal hernia very clearly (Fig. 4).

An extrapleural thoracoplasty was done. Because of blockage of bronchial secretions due to the bronchial stenosis resulting in a septic critical condition of the patient, external drainage of the huge intrapulmonary cavity was done. After drainage the patient improved greatly and the huge intrapulmonary cavity gradually, in the course of four months, shrank to approximately one-fifth of its preoperative size. Some degree of mediastinal herniation persisted.

Comment. This patient had large anterior and posterior mediastinal herniae on the side of a greatly shrunken, fibrotic, tuberculous lung containing a huge cavity, the bronchus of this lung being greatly stenosed.

Case v. O. C. (No. 366047), female, aged twenty-six, was admitted November 25, 1935. Pulmonary tuberculosis had been diagnosed in 1931. In 1934 left pneumothorax was started, but adhesions prevented a good collapse, fluid developed, and the pneumothorax was abandoned.

Physical examination showed the trachea to be deviated to the left and there was a slight lag on respiration on the left. The left chest was dull throughout, and there were decreased breath sounds.

Bronchoscopy revealed early non-ulcerative and non-stenotic tuberculous tracheobronchitis.

Roentgenograms showed the heart and mediastinum to be shifted to the left, where there was more or less homogeneous clouding over the entire pulmonary field. The left diaphragm was elevated. There were two cavities in the left upper lateral pulmonary field. Films made with the Potter-Bucky diaphragm showed medially two semicircular areas of decreased density; one, which was stereoscopically anterior, extended from the level of the sternoclavicular joint to about the fifth cartilage, and the other, which was stereoscopically posterior, extended from the level of the seventh dorsal vertebra to the eleventh dorsal vertebra (Fig. 5). These undoubtedly represented herniae from the right lung through the anterosuperior mediastinal weak space and the postero-inferior mediastinal weak space, respectively.

A thoracoplasty was done. Films on discharge showed that the anterior mediastinal hernia still persisted to a considerable degree; in fact, it seemed to occupy a considerable portion of the upper part of what remained of the left hemithorax (Fig. 5). The posterior herniation had receded considerably.

Comment. This is a case of large anterior and posterior mediastinal herniae in a patient who had once had pneumothorax. In this case the previous pneumothorax was probably a factor in the development of the mediastinal herniation. The anterior hernia was still quite large after thoracoplasty. The patient is free of symptoms.

Case vi. I. W. (No. 388442), female, aged

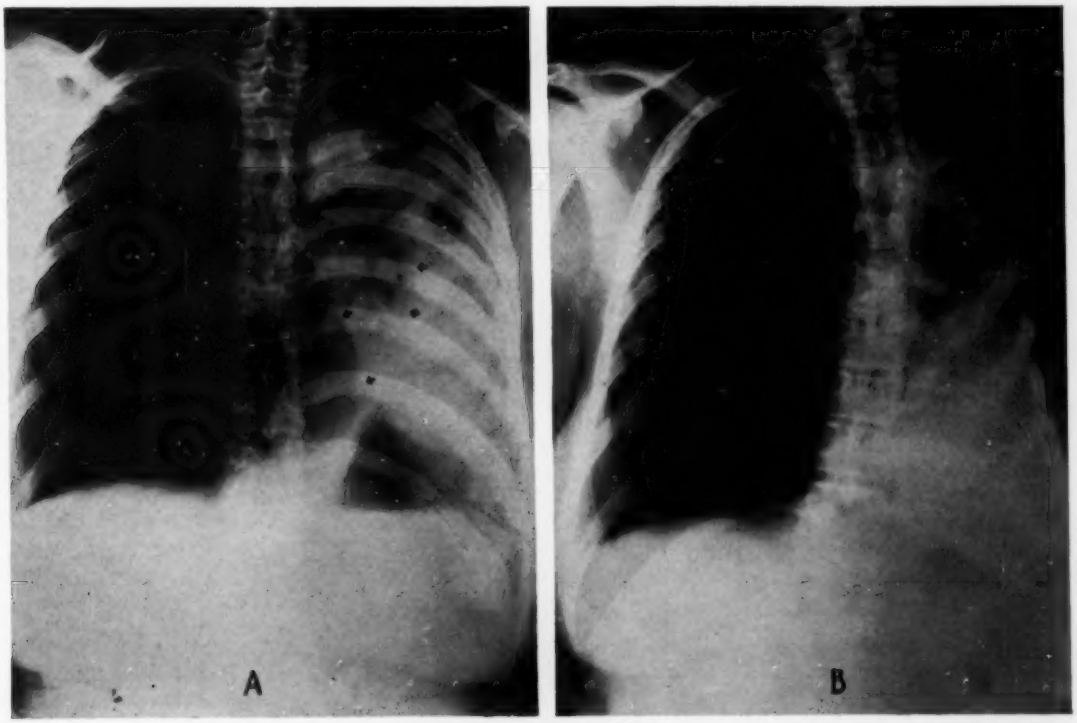

Fig. 5. Case v. *A*, upper three arrows indicate the anterior mediastinal hernia from the right. Lower two arrows indicate the border of a posterior inferior mediastinal hernia. Far advanced left pulmonary tuberculosis. *B*, arrows indicate the border of the persistent anterior mediastinal hernia after thoracoplasty. Note correction of the distortion of the left bronchus.

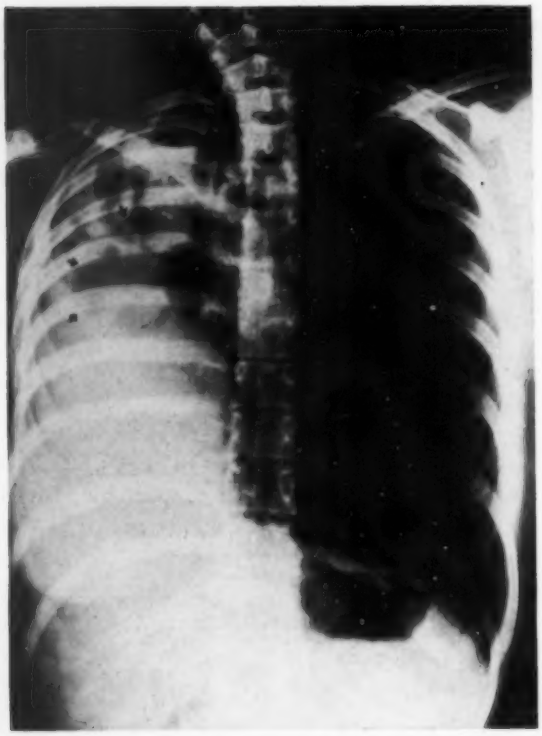

FIG. 6. Case VI. Arrows indicate the border of a herniation by the left lung through the anterior mediastinum. Far advanced tuberculosis of the right lung with bronchial stenosis.

thirty-two, was admitted August 31, 1936, with a five-year history of cough which was occasionally productive of a small amount of sputum. At times during the past four years she had noted difficulty in breathing; the attacks resembled asthmatic episodes. Three years ago she had severe pleurisy on the right side. Pneumothorax had never been attempted.

Examination revealed tracheal deviation to right. There was decreased tactile fremitus on the right. The breath sounds on the right side were tubular in quality with an expiratory whistle. The apex beat was palpated at the right of the sternum. The left border of cardiac dullness was just to the right of sternum. Heart sounds were heard best in the right chest.

Bronchoscopy revealed that the trachea was deviated sharply to the right and the carina was rotated clockwise. In the right bronchus, just below the carina, there was a fibrous stenosis. A diagnosis of fibrostenotic tuberculous bronchitis of the right stem bronchus was made.

Roentgenograms showed the heart and mediastinum to be displaced markedly to the right. There was gross fibrosis and atelectasis of the right pulmonary field with multiple excavations in the upper portion. The left lung had herniated through the anterior medias-

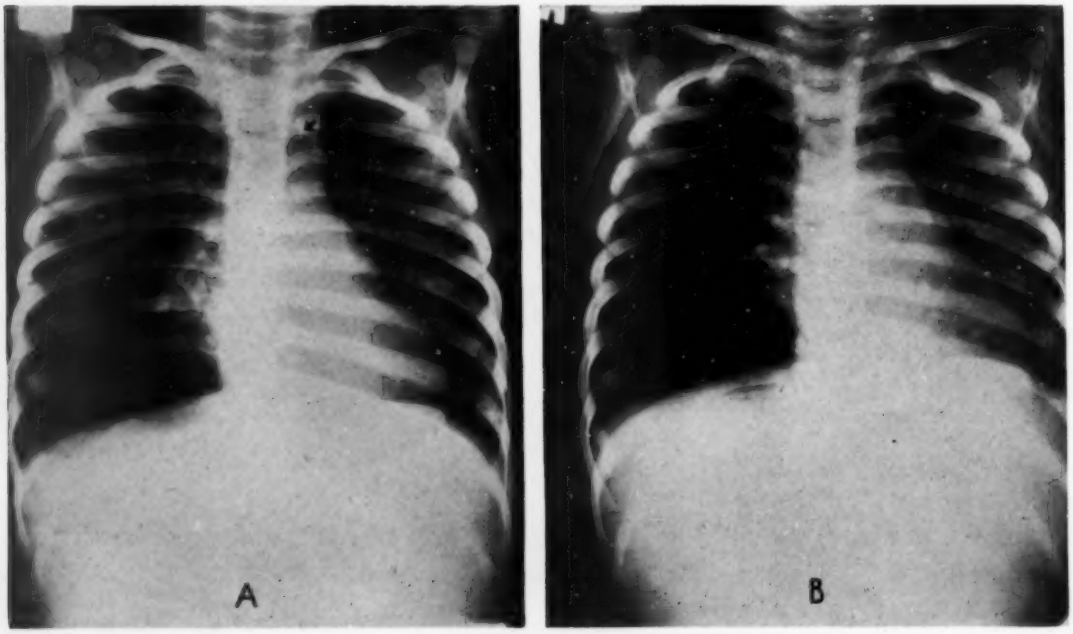

FIG. 7. Case VII. *A*, anterior mediastinal hernia from the right associated with atelectasis of the left lower lobe (obscured by cardiac shadow). Hernia accentuated in inspiration. *B*, herniation reduced in expiratory phase.

tinal weak place; the herniation is seen best on Potter-Bucky roentgenograms (Fig. 6).

An extrapleural thoracoplasty was done. The difficulty in breathing which had been present before operation was greatly improved after thoracoplasty. The mediastinal deviation and herniation were much less after operation.

Comment. This patient had an anterior mediastinal hernia secondary to marked fibrosis and atelectasis of the right lung.

Case vii. R. M. (No. 402024), male, aged twenty-two months, was admitted May 10, 1937. Three months previously the child had aspirated a peanut. Bronchopneumonia developed subsequently. Since that time there had been cough and fever. Physical examination revealed dullness, diminished breath sounds, and râles over the right upper lobe and the left lower lobe.

Roentgenograms of the chest showed infiltration in the right lung. The left lower lobe was atelectatic. There was herniation of the right lung through the anterior mediastinal weak place. This herniation was present chiefly on inspiration (Fig. 7). The lateral film clearly showed the herniation.

The atelectasis of the left lower lobe cleared up gradually after bronchoscopy. The mediastinal herniation slowly disappeared.

Comment. In this case an anterior mediastinal hernia developed secondary to atelectasis of the left lower lobe. The fluctuations in the size of the hernia with respiration are well shown on the roentgenograms.

SUMMARY

1. Mediastinal hernia may occur in the absence of pneumothorax.

2. There are three "weak places" in the mediastinum through which herniation may occur.

3. Pathological processes causing a considerable diminution in the volume of one lung tend to induce herniation of the opposite lung through the mediastinum. The more common etiological factors are tuberculosis with advanced pulmonary fibrosis, and lesions producing bronchial obstruction with resultant atelectasis.

4. The diagnosis of mediastinal hernia depends on roentgenologic findings. Films exposed with the Potter-Bucky diaphragm are a great aid in the establishment of a diagnosis.

5. Knowledge of the existence of mediastinal herniation may prevent inadvertent injury to the herniated normal pleura at the time of an intrathoracic operation or induction of pneumothorax.

6. Mediastinal herniation must be considered in the interpretation of roentgenological shadows.

I wish to express my grateful appreciation to Dr. John Alexander and Dr. Carleton B. Peirce for their many helpful suggestions.

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THE MENINGIOMAS

FROM A ROENTGENOLOGICAL VIEWPOINT*

By CHARLES WADSWORTH SCHWARTZ, M.D.
NEW YORK CITY

SINCE the memorable article of Sosman and Putnam was written on this subject in 1925, our conceptions of these tumors have changed but little, but that little seems enough, together with the added material at hand, to warrant a recapitulation of the salient points regarding the roentgenographic diagnosis, treatment, and underlying pathology of the now considered group of tumors known collectively as the meningiomas.

As with all forms of roentgenographic diagnosis, one should be familiar with what is known regarding the pathology of the lesion in order properly to interpret the shadows seen on the film. The pathology of the meningiomas has been carefully studied by several authorities since Cushing, in 1922, suggested the name "meningioma" for the until then called "dural endothelioma." Bailey has divided the meningiomas into several groups and names them according to the predominant cell characteristics. He has designated them as follows: (1) psammomatous, (2) mesenchymal, (3) sarcomatous, (4) osteoblastic, (5) lipomatous, (6) angioblastic, (7) fibroblastic, (8) melanoblastic, (9) meningotheliomatous. We could hardly expect to differentiate all these types in the roentgenogram for even under the microscope they may at times be seen to overlap and merge one into the other. We can, however, occasionally differentiate a few of them, as will be shown when we come to a discussion of the diagnostic criteria.

The meningiomas as a group constitute about 13 to 15 per cent of all intracranial tumors, the percentages varying slightly in different neurosurgical clinics. They are, on the whole, very slowly growing and occur grossly in two chief forms: a roughly globular, well-encapsulated, rather hard type, and a soft, poorly encapsulated, flat and often widespread type. Neither of these metastasizes or invades the brain tissue, although the flat, soft, so-called "en plaque" type may surround brain structures, and it is also apt to invade the overlying bone which is then stimulated to produce the hyperostoses which are so characteristic of these tumors. The terms used by Bailey to designate the various members of the meningioma group clearly indicate their several basic histological structures. It might be noted, however, that the meningotheliomatous and psammomatous types are very similar, the latter differing from the former in its cellular arrangement, which is characteristically in "whorls," and it is within these whorls that central degeneration occurs with the deposit of calcium. These two types comprise about 90 per cent of the entire group, and in neither of them do the cells contain mitotic figures.

The angioblastic type accounts for about 2 per cent of the entire group. As the name implies, it is very vascular and is the most rapidly growing of them all, and shows the greatest tendency to recur. The cells forming this type of meningioma contain many mitotic figures. The osteoblastic variety is rare and when found is usually in the spinal canal. Bailey points out that the bony formation is evidently of membranous origin. The sarcomatous variety is usually widespread and often forms groups of cells about the blood vessels, thus forming the so-called peritheliomas. The cells are frequently found to contain mitotic figures, which is true of all the meningioma types with the exception of the osteoblastic variety and the two most common types, the psammomatous and the meningotheliomatous.

Most authorities agree that the menin-

* From the Department of Radiology, Neurological Institute of New York.

giomas are of connective tissue origin, and that the majority of them originate from the arachnoid. Elsberg has convincingly pointed out that many of them have a dural origin so that it is probably safe to conclude that they nearly all originate either from the arachnoid or from the dura mater. They have definite sites of election, a fact to be continually borne in mind when examining roentgenograms of the skull. These sites of election and the percentage of tumors found in each have been excellently tabulated by Elsberg. His tabulation follows:

Over the cerebral convexities (not attached to longitudinal sinus or falx)	35.3%
Parasagittal (attached to longitudinal sinus or falx)	24.5%
Temporal or occipital (attached to dura of base)	12.7%
Attached to dura of sphenoid ridge or cribriform plate	11.7%
Occipital (attached to lateral sinus)	1.9%
Attached to dura of tuberculum sellae	1.9%
Attached to dura near cavernous sinus	1.9%
Subtentorial	8.8%
Multiple	0.9%

From this table it can be seen that wherever the arachnoid granulations are numerous, these tumors are apt to occur, and also where the cerebral veins enter the large venous sinuses is a not uncommon place to find them. In addition, it might be noted that of those tumors found over the cerebral convexities, the majority occurred anterior to the fissure of Rolando, a characteristic pointed out by Cushing in 1922.

The meningioma is definitely a tumor of adult life, the greatest number occurring in persons between the ages of forty and fifty years. There has, however, been a case reported by de Martel in a child of no greater age than nine years, but cases in young people are rare. Due to the fact that the meningiomas grow slowly and displace rather than invade brain tissue, their onset is apt to be insidious and not infrequently follows a definite history of trauma. For years the patient may exhibit vague but progressive mental changes with or without headache, which makes an early diagnosis at times quite difficult, but less so if the possibility is not lost sight of. It is because of the reluctance of most physicians and all patients to consider the possibility of intracranial pathology that these tumors often reach enormous sizes. And inasmuch as the meningioma is a tumor quite amenable to successful surgery it is unfortunate that early diagnosis cannot more frequently be made, for a large tumor may and frequently does present the surgeon with a well nigh insuperable task to safely and completely remove it. Certainly every patient with any sign of mental change, with or without headaches, should be given the benefit of a careful roentgenographic examination of the head, and this does not mean the taking of one or two films and then holding them up to a window, a method which is all too often used.

Through the kindness of Dr. Byron Stookey, the records of the Surgical Department of the Neurological Institute were made available for this study. These records were gone over for the past five years and all the cranial meningioma cases which also had complete roentgen studies were collected. This included almost the entire group as only a few emergency cases were found to have been operated upon without adequate preoperative roentgen studies.

In the following discussion of this group of cases, of which there were 129, it must be borne in mind that they were all operated upon shortly after the roentgen examinations had been completed. Therefore the percentages given are of necessity representative only of cases which were far enough advanced to be potentially surgical, although in several cases, particularly those with lesions directly above the tuberculum sellae, the tumors were very small.

Of this group of 129 cases, 102 cases, or 79 per cent, showed definite evidence in the roentgenograms of the presence of intracranial pathology, and in all but 26 a diagnosis of meningioma was possible. The exact location and extent of the tumor was however not infrequently uncertain, so

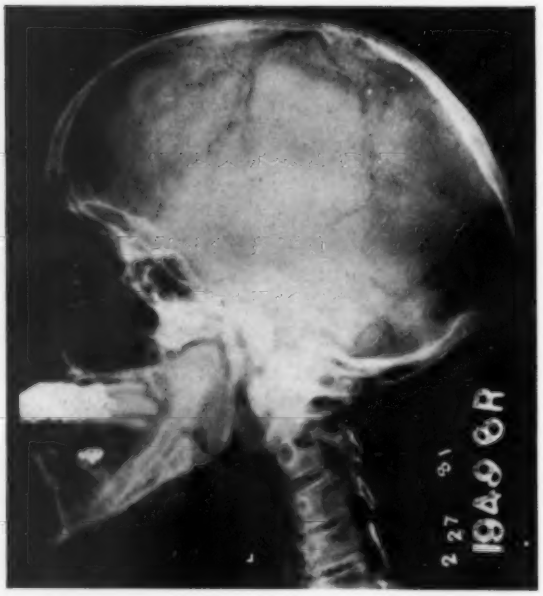

FIG. 1. Hypervascularity associated with a parasagittal tumor.

that in 56 cases encephalography was resorted to; all of these cases resulted in positive findings. It should be noted, however, that in 10 cases the exact type of tumor present could not be stated. In 65 cases, or approximately 50 per cent, the sella turcica showed varying degrees of atrophy, so much so that in 2 cases a diagnosis of pituitary adenoma was suggested but this was rectified when roentgen studies were made after gas injection. In about 25 per cent a recognizable degree of localized hypervascularity was present and in 33 per cent a localized hyperostosis was noted, but in only 0.5 per cent was a localized bone atrophy seen due to direct pressure from the tumor itself. In only 2 per cent of the cases was there sufficient calcium in the tumor to cast a recognizable shadow on the film. The pineal body was seen to be calcified in only 33 per cent of this group; this is odd as the general average is about 55 per cent. Such a finding is undoubtedly mere chance and has nothing to do with the presence of a meningioma. Of this group of calcified pineals, 70 per cent were shown to be displaced away from the location of the tumor, and 30 per cent remained within the limits of the normal zone as measured by the charts devised by Vastine and Kinney.

DIAGNOSTIC CRITERIA

The meningiomas occurring over the convexities of the cerebrum are vastly more common anterior to the fissure of Rolando. They are apt to be of the flat meningotheliomatous type, and this type is prone to incite the overlying bone to produce a spiculated hyperostosis with an accompanying hypervascularity. The involvement of the bone first consists in the laying down of new bone parallel to the two tables which then become of greater density as seen in the roentgenogram. Soon, however, the hypertrophy begins to occur in the form of spicules which are at right angles to the tables of the vault, and in this way produce the tumors not infrequently felt under the scalp, which may also contain actual tumor tissue. These changes are evidently due to invasion of the bone by tumor cells. The hypervascularity may be widespread or extremely localized, but in either case a careful comparison with the opposite side will

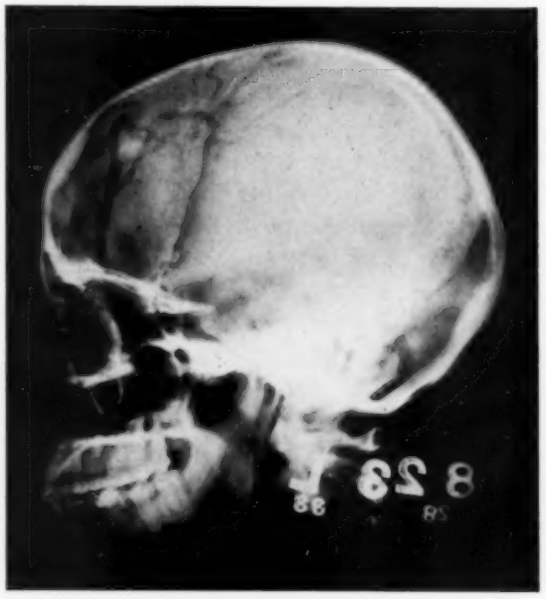

FIG. 2. Hypervascularity in association with a frontal meningioma. This type of vascularity might easily be confused with vascular changes produced by an arteriovenous angioma.

usually permit of its recognition. Occasionally the pineal gland will be displaced and there may be slight atrophy of the sella turcica, chiefly involving the dorsum sellae, but there will usually be no distortion.

These changes must be differentiated from the very occasional osteoma, an arteriovenous angioma, a hemangioma of bone, fibrocystic disease with giant cell tumefaction, and from osteomyelitis of whatever etiology. The osteoma will usually involve both tables so that even in the most carefully taken profile films the tables will be difficult to differentiate, whereas with the meningioma the tables can often be distinguished. Rarely, however, a meningioma will destroy bone so that portions of either table may be absorbed, and not uncommonly the hypertrophic reaction will make the differentiation of the tables impossible. With the osteoma there would be no hypervascularity which is not infrequent in the presence of a meningioma. The actual bone formation may be indistinguishable but if spiculation can be made out it is almost certainly not an osteoma, and the history is usually significant.

The hypervascularity resulting from the presence of an arteriovenous angioma may

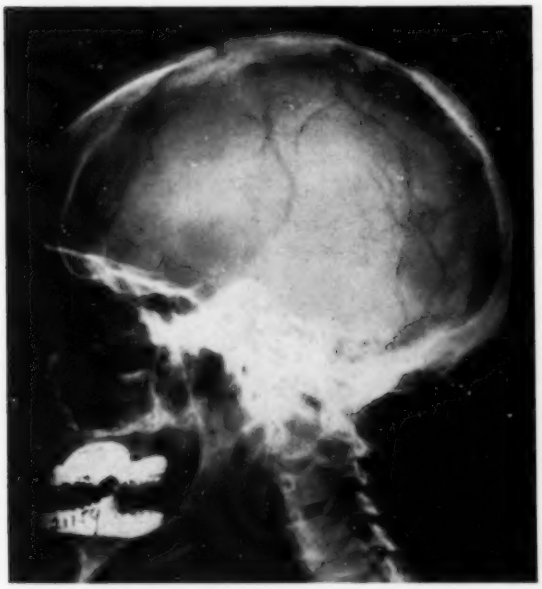

Fig. 3. Hypervascularity plus slight hyperostosis due to the presence of a parasagittal tumor.

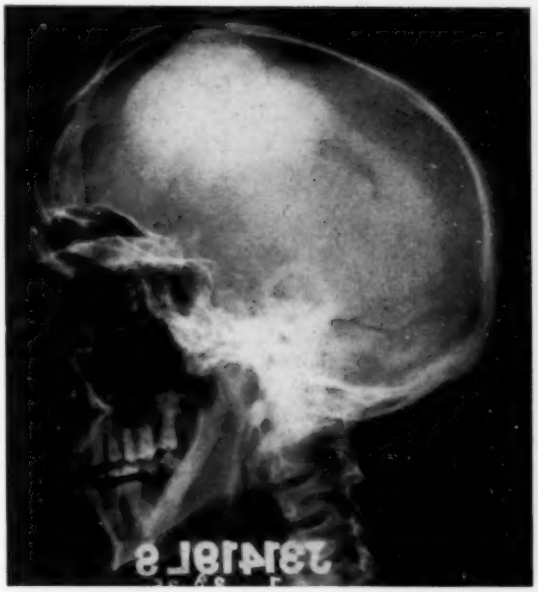

Fig. 4. Hyperostosis combined with calcification in a large parasagittal meningioma. The pineal gland is displaced but the sella turcica is intact.

duplicate the hypervascularity due to a meningioma, but fortunately the angiomas are prone to calcify and the calcification will usually be found in the blood vessel walls, so that the deposits will be in parallel streaks. Calcification, when it occurs in a meningioma, which it frequently does, is usually seen as a film-like deposit and therefore quite amorphous. An angiomatous meningioma may present a condition practically indistinguishable from an angioma. The bone reaction to these two conditions may be very similar and the history may also be confusing. If, however, one is able to hear a bruit by using a stethoscope, the chances would be vastly in favor of the lesion being an angioma, which of course is not a true tumor. It must be noted, however, that a bruit can occasionally be heard in the presence of an angiomatous meningioma. The pineal gland may be displaced with either type of lesion.

A hemangioma of the vault might at times simulate the changes caused by a meningioma, but the lesion is usually more definitely circumscribed and there are no large vessel channels leading to it. Spiculations may be present with both, but true

FIG. 5. Hyperostosis anterior to the tuberculum sellae produced by a tumor arising along the olfactory groove.

profile films will usually show the hemangioma to have produced a fusiform swelling of both tables due to the lesion being chiefly in the diploe, and it would be rare indeed to find the pineal body displaced by a hemangioma of the vault.

Fibrocystic disease can closely simulate the bony changes of a meningioma and at times a differentiation may be difficult. The fibrocystic disease, however, usually involves chiefly the diploe and outer table which may be partly absorbed and the resultant swelling will be seen to be rather fusiform. There is not, as a rule, any hypervascularity or displacement of the pineal gland.

Osteomyelitis, particularly luetic, may be confused with the roentgen manifestation of a meningioma, but the history will usually be a great help in a differentiation. The osteomyelitis is usually destructive and involves the outer table; vascularity is, as a rule, unchanged, and the pineal gland will be normally situated.

The parasagittal tumors are usually more bulky than those occurring over the convexities, but are of the same or a very similar histological structure. Tumors in this location are much more apt to give rise to a localized area of hypervascularity which at times may be very small and difficult to differentiate from the vascularity often seen in the vicinity of the dural lacunae, on either side of the longitudinal sinus. True pathological hypervascularity will usually be seen as few or many rather tortuous small and large channels which have perforated the bone so that it is somewhat honeycombed. And in addition, channels will often be seen leading to this area which have no counterparts on the opposite side. Occasionally, as has already been mentioned, calcification may be visible, which almost invariably will be in the form of an amorphous, hazy mass. The angiomatous meningioma may contain streaky deposits of calcium. Not infrequently parasagittal tumors will displace the pineal gland, and oddly enough the tumors may attain large size without producing any changes in the sella turcica. When sella turcica changes do occur, they do not differ from those produced by gliomas or other intracranial tumors, even at times closely simulating an

FIG. 6. Hyperostosis caused by a meningioma of the sphenoid ridge and involving the tuberculum sellae.

intrasellar tumor. General signs of increased intracranial pressure are frequently absent.

Tumors occurring in the temporal region are not infrequently found originating from the dura covering the petrous pyramid, or attached to the wall of the superior petrosal sinus. When found in this location, the diagnosis is often difficult from the roentgenogram alone as a meningioma may exist for some time without producing any demonstrable bony change. It is, however, frequently possible to recognize a unilateral atrophy of the sella turcica which would of course point to a lesion on the atrophic side. The pineal gland is often displaced but signs of generalized increased intracranial pressure are frequently absent. Increased vascularity in this location is difficult to recognize unless the lesion involves the squamous portion of the temporal bone, and occasionally the only demonstrable change will be a small area of bone atrophy involving the petrous ridge. This could easily be confused with a malignant lesion such as carcinoma, but the history would help greatly in a differentiation. An epidermoid or a neurinoma of the eighth nerve sheath might produce changes and even a clinical picture which would exactly simulate a meningioma. Often, however, a meningioma in this location will give rise to a marked degree of bony overgrowth which could only be confused with an osteoma. The bony changes due to a meningioma, however, do not by any means represent the extent of the tumor, so that the clinical manifestations would usually indicate a lesion greater than would be expected from the bone changes alone.

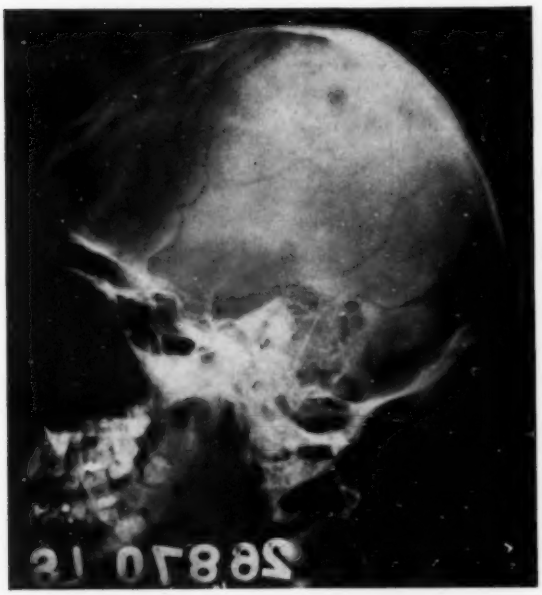

Fig. 7. Osteitis fibrosa cystica of the parietal region. A condition which might easily be confused with a bone change due to a meningioma. Note that there is no increase in vascularity.

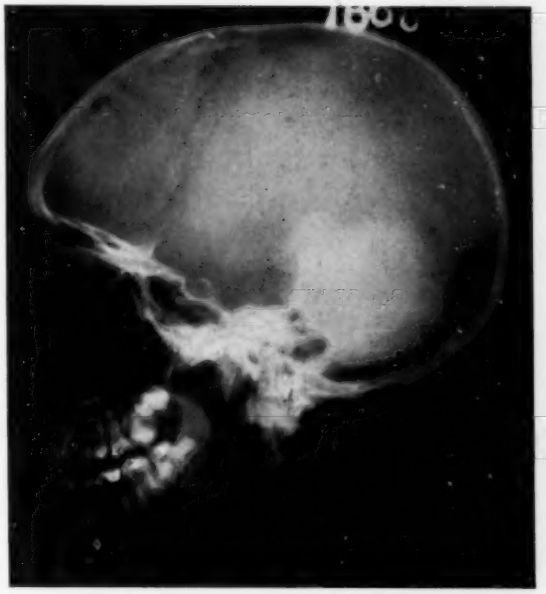

Fig. 8. Hyperostosis due to a meningioma arising from the immediate vicinity of the petrous ridge.

Meningiomas originating along the sphenoid ridge frequently produce a marked hyperostosis with an accompanying enlargement of the superior orbital fissure. The tumor mass may invade the orbit and result in a unilateral exophthalmos, sometimes of marked degree but usually nonpulsating. Atrophy of the sella turcica is not uncommon in the presence of sphenoid ridge tumors. The atrophy may be unilateral and is due to localized pressure because rarely will a tumor in this location produce any general rise of intracranial pressure. The sphenoid ridges can usually

be best studied in anteroposterior or posteroanterior stereoscopic views, but the lateral stereoscopic views should never be omitted. In this connection it might not be amiss to mention the fact that the normal sphenoid ridges often appear asymmetrical, particularly their inner portions. A slightly off center film will make the two sides appear markedly different. Therefore, one must be careful not to misinterpret asymmetry of the ridges as atrophy and draw false conclusions. It is, however, fair to assume that any bony overgrowth seen involving a sphenoid ridge is, until proved otherwise, a meningioma. It may also be noted here that the posterior orbital walls may at times be of different densities. Films of sufficient clarity and detail will usually permit a differentiation between healthy bone and bone which is pathological.

Meningiomas involving the olfactory groove and those of the sphenoid ridges may merge one into the other. Those involving the cribriform plate, however, are prone to produce bony overgrowth which is usually irregular in outline and may extend both above and below the plate. Anosmia is a common early symptom of a tumor in this location. And this symptom should not be difficult to recognize in its early stages by making use of the newer methods of testing smell, devised by Elsberg. As in the case of the tumors of the sphenoid ridge, any overgrowth of bone along the olfactory grooves of the ethmoid should be considered as evidence of a meningioma. It might be of interest to note here that one of the first, if not the first, meningioma to be successfully removed and reported, was a tumor of the sphenoid ridge removed by F. Durante who reported his case in 1887.

Meningiomas arising from the walls of the lateral sinuses in the occipital region are relatively rare and often very difficult to recognize. They are much more likely to produce signs of increased intracranial pressure than are lesions situated in the locations already mentioned, and are also apt to displace the pineal gland when the tumor attains an appreciable size. Bony overgrowth is not common, nor is demonstrable hypervascularity. Calcification, however, is as common as it is in lesions found in the more common sites. It is unfortunate but true that frequently in the presence of a meningioma in the occipital region we are able merely to state that a tumor is present of unknown type.

Meningiomas originating from the dura of the tuberculum sellae, immediately above the sella turcica, and from the walls of the cavernous sinuses, are often difficult to diagnose from the usual roentgen examination. If calcification is present it is just as apt to be in a glioma, a blood vessel anomaly, or a craniopharyngioma. Atrophy of the sella turcica may or may not be a factor. In the presence of a glioma roentgen differentiation may be impossible. With a blood vessel anomaly, usually an aneurysm, we would expect one or more of the three cardinal signs of such a lesion, namely curvilinear streaks of calcification, unilateral atrophy of the sella turcica and homolateral enlargement of the optic canal. A craniopharyngioma is essentially of congenital origin, so it would be unexpected in a patient of "meningioma age." Any bony hypertrophy of the tuberculum sellae should be considered as strong evidence of the presence of a meningioma. Frequently, however, tumors in this location can only be detected by the most careful encephalographic studies, which not infrequently show slight distortions of the cisternae interpeduncularis, chiasmatis and lamina terminalis.

The meningiomas occurring subtentorially are usually indistinguishable from any other form of intracranial tumor in a similar location. Increased intracranial pressure is, of course, a frequent finding. Calcification, if present, would be insufficiently characteristic to permit of a differential diagnosis. The history might be of some aid, but usually we must be content merely to state there is evidence of a tumor.

Multiple meningiomas, it is true, are rare, but we must not be misled when mul-

tiple manifestations are seen, into thinking that meningiomas occur only as single lesions. It might be well to mention a fact often lost sight of, that multiple intracranial lesions do occur in other conditions as well as in meningiomas. When we find evidence of an intracranial lesion we are so apt to concentrate on this evidence that the remainder of the skull is not searched as diligently as it should be.

Radiotherapy of the meningiomas is extremely disappointing. The results are usually poor and such a tumor should not be treated without first permitting the patient to have expert surgical attention. The efficacy of radiotherapy for the various meningiomas can be predicated on the same grounds as for the treatment of the gliomas, which is according to the presence or absence of appreciable numbers of cells containing mitotic figures. As the varieties containing cells with mitotic figures are much more radiosensitive than those without, it will be seen that as 90 per cent of the meningiomas are of the meningotheliomatous and psammomatous types which contain practically no mitotic figures, the majority of the meningiomas would not be expected to respond satisfactorily to irradiation. If, however, the surgeon feels that he was unable to remove the tumor completely at operation, I would strongly advocate the institution of roentgen therapy in a total amount of from 2,500 to 3,500 r in divided doses with intervals of twenty-four hours, or if that is not practical then with intervals of forty-eight hours because, as with the non-radiosensitive gliomas, the recurrence of the tumor may be forestalled or at least slowed up. But as these tumors grow so slowly, the exact evaluation of radiotherapy is difficult, and much work remains to be done before we can be certain that we have exhausted the possibilities of radiation therapy.

The other forms of the meningiomas, with the exception of the osteoblastic type, contain cells with mitotic figures, so that radiation therapy, after surgery, would be definitely indicated unless the surgeon felt sure the operative removal was complete. The angioblastic type is probably the most radiosensitive and, as has been mentioned before, it is the most apt to recur; hence when such a tumor is found one should apply radiation regardless of the extent of the operation, on prophylactic grounds only, because here we may entertain real hopes of being able to forestall a recurrence.

SUMMARY

A brief résumé has been given of the chief characteristics of the group of tumors known as the meningiomas. The roentgenographic diagnosis of tumors occurring in their various sites of election has been discussed, together with a final note on the rationale of radiotherapy.

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PERSISTENT RIGHT-SIDED AORTIC ARCH

By L. H. GARLAND, M.B.

From the Division of Radiology, Department of Medicine, Stanford University Medical School
SAN FRANCISCO, CALIFORNIA

PERSISTENT right-sided aortic arch is a rare and interesting congenital anomaly which occasionally is the cause of dysphagia or dyspnea in adult life. Various types and modifications of this anomaly have been reported,[4,12] and it appears that a common type is one in which the aortic arch passes to the right of and *behind* the trachea and esophagus, and thence downward slightly to the right of the thoracic spine, i.e., right-sided retroesophageal aortic arch. In the words of Fray:[4]

> The diagnosis is seldom established during life although it is the easiest of all the congenital anomalies of the circulatory system to recognize with certainty. This can be accomplished immediately in practically all cases in which a complete roentgenologic examination of the heart can be made. The importance of this becomes more manifest when we realize that the diagnosis cannot be established with any reliance by the usual clinical procedures. All cases familiar to the writer, which have been identified prior to the findings of the autopsy table, were diagnosed through the use of the roentgen ray. However, there is a strong likelihood that many cases of right aortic arch have passed through the hands of the roentgenologist without having been recognized. The factors responsible for this condition are not hard to find: (1) Elimination of fluoroscopy from the examination; (2) restriction of the radiographic examination to the postero-anterior film; (3) failure to consider barium studies of the esophagus as a part of the cardiac examination—particularly in obscure cases.

ANATOMY

The development of this anomaly may be understood by a brief consideration of the fetal pre-aortic structures. In a five-week old embryo there are five pairs of aortic arches; a transitory pair of arches subsequently appear between the most caudal sets of these five, so that strictly speaking there are six pairs of aortic arches at a certain stage of development. These arches connect the primitive ventral aorta with the primitive dorsal one. The normal adult aortic arch is merely the left half of the fourth embryonic aortic arch.

The first two arches, on each side, disappear, and their ventral roots become the external carotid arteries of the adult. The ventral root of the third arch becomes the common carotid, while the third arch and the dorsal roots of the first and second arches are transformed into the internal carotid. The ventral root of the fourth arch on the right side becomes the innominate artery, and the right fourth arch forms the proximal part of the right subclavian artery. The remainder of the right subclavian is developed from the seventh right somatic intersegmental artery. The ventral root of the left fourth arch and the arch itself form the arch of the aorta. The fifth arch, as already stated, is quite transitory; it leaves no remains, therefore it is not necessary to speak of any part of the ventral stem as its ventral root. The ventral part of the sixth arch on the right side becomes the extrapulmonary part of the corresponding pulmonary artery. On the left side it practically disappears. On the right side the dorsal part disappears, but on the left side it persists, till birth, as the ductus arteriosus, which connects the pulmonary artery with the aorta, and after birth it is converted into the ligamentum arteriosum. The truncus arteriosus is cleft into two parts by a spiral septum; one part, which remains continuous with the ventral roots of the fourth arches and therefore with the innominate artery and the aortic arch, becomes the ascending aorta, and the other, which remains associated with the sixth arches, becomes the stem of the pulmonary artery.[3] These changes are shown diagrammatically in Figure 1.

It is noteworthy that in birds the fourth right fetal arch normally becomes the aor-

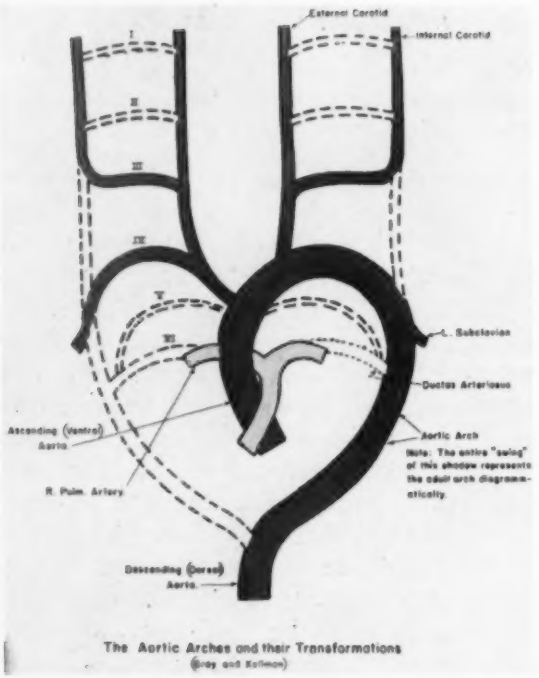

FIG. 1. Diagram of the fetal aortic arches and their subsequent counterparts. Note: the entire "arc" of the main aortic shadow in this diagram is an elongated representation of the adult arch. (Modfied from Gray and Kollman.)

tic arch, while both fourth arches persist, forming the double aortic arch seen in these animals.[11]

TYPES OF RIGHT-SIDED AORTIC ARCH

Both halves of the fourth aortic arch may persist into adult life; in such cases the right arch passes behind the esophagus while the left passes in front of it, the esophagus thereby appearing to perforate the aortic arch. Right-sided aortic arch may be due to persistence of the right fourth fetal arch or to situs inversus.

Fray[4] lists the following types:

Right aortic arch, with persistent left aortic diverticulum.
Right aortic arch, with persistence of ventral portion of left arch.
Double aortic arch.
Persistent right aortic arch.
Right aortic arch, with separate origin of main branches from right aortic arch.
Right aortic arch, with symmetrical reversal of vessels.

The following are the findings which he lists with these types:

Type	Position of the Esophagus	Course of the Descending Aorta
Right aortic arch with persistent left aortic diverticulum	Displaced anteriorly	Passes to right of normal position
Right aortic arch with persisting ventral left arch	Displaced anteriorly	Passes to left behind esophagus
Double aortic arch	Variable	Passes downward to left of mid-line.
Persistent right aortic arch	Normal	Normal
Right aortic arch with separate origin of main branches	Normal	Anomalous
Right aortic arch with symmetrical reversal of vessels	Normal	Anomalous

DIAGNOSIS

The diagnosis of right-sided aortic arch can usually be made by the following roentgen findings:

1. Right upper paramediastinal shadow (visible in the posteroanterior projection).

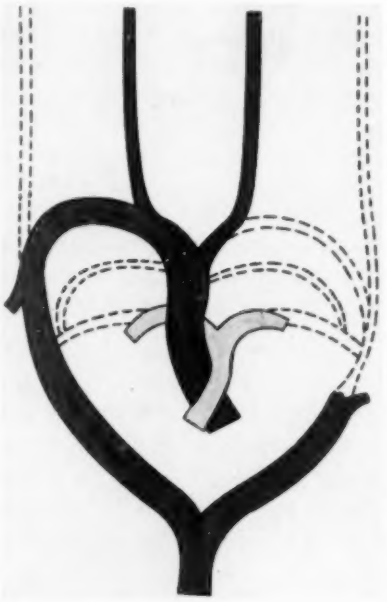

FIG. 2. Persistent right aortic arch, diagrammatic representation.

This shadow lies high up, at the level of the sternoclavicular articulation; it is variable in width and degree of pulsation. It is produced largely by the right aortic arch.

2. Apparent hypoplasia or complete absence of the normal left upper paramediastinal shadow—the normal aortic arch or "knob." In cases with a persistent left aortic diverticulum this shadow may, however, be present.

3. Presence of an oval or rounded soft tissue shadow, in the mid-plane of the upper mediastinum (visible in oblique projections). This may appear to be about the size of a golf ball and may not be observed to pulsate. It is produced by axial projection of the anomalous arch.

In connection with the diagnosis of anomalous aortic arches, the following observations taken from Golden's recent book on "Roentgenology" are interesting, although we do not agree with his observation of "well marked pulsation."

The anterior view reveals a well-marked pulsating vascular shadow to the right, which extends upward and slightly outward toward the right sternoclavicular junction. In curving to the left and medially, a more or less pronounced aortic knob is formed. The left contour is either rather straight, or more often is slightly convex at, or just below, the level of the right-sided aortic knob. The trachea and the esophagus (the latter as demonstrated by barium paste) both deviate to the left at the level of the right-sided aortic knob, sometimes only slightly, although more often in a quite pronounced manner. The right anterior oblique view shows the visible portion of the aortic shadow in front of the trachea to be quite small. Trachea and esophagus, at this level, deviate forward. Back of trachea and esophagus there is noticed a round mass which is represented by the aortic arch; it may have a denser and smaller round area toward the front, which corresponds to a diverticular enlargement represented by the root of the left dorsal aorta.

An absence of a (left-sided) aortic knob is also observed in cases with coarctation of the aorta; in hypoplasia of the aorta, as in combination with an interatrial septal defect; in certain types of transposition of the large vessels; with persistence of a left-sided superior vena cava; and (*vide supra*) with a mirror type right-sided aortic arch. The typical deviation of trachea and esophagus has often been erroneously interpreted; aneurysm and mediastinal glandular mass were considered to be present.

DIFFERENTIAL DIAGNOSIS

The following lesions could conceivably be confused with right-sided retroesophageal aorta—although we have observed no cases and no case reports in which such occurred: (*a*) small circumscribed upper mediastinal tumors, located posteriorly; (*b*) mediastinal abscesses; (*c*) large vertebral exostoses.

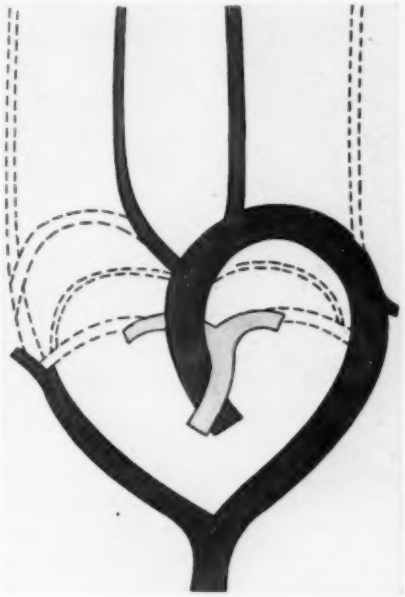

Fig. 3. Anomalous right subclavian artery, arising from the descending portion of the aortic arch; this is retroesophageal in position.

All of these lesions can be differentiated from right-sided retroesophageal aorta by careful roentgen examination, with demonstration of a normally located aortic arch, and, in some cases, by absence of pulsation in the tumor and of a right descending paravertebral (aortic) shadow. It is to be noted that in some persons the left anterior oblique projection of the barium-filled esophagus may present an indentation which may mislead the observer into diagnosing retroesophageal pressure. Roentgenoscopic

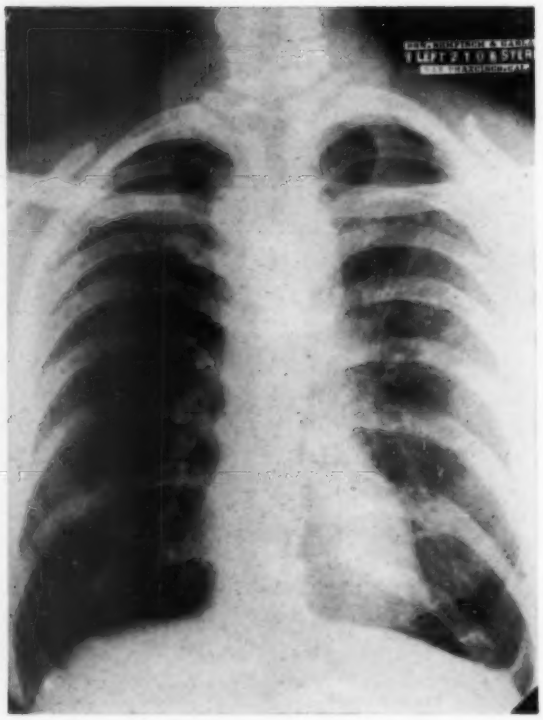

FIG. 4. Case 1. High right-sided aortic arch. Posteroanterior film. Observe the right upper paramediastinal shadow and the shallow or "hypoplastic" left aortic knob. (Note: the small metallic shadow just below the left sternoclavicular joint and the small left apical pneumothorax are incidental unimportant findings.)

observation with careful rotation of the patient will prevent this error being made.

CASES REPORTED IN THE LITERATURE

There appear to be approximately 113 cases of this interesting anomaly on record. In 1932 Blackford, Davenport and Bayley[1] recorded that there were approximately 100 cases on record, most of them being identified only post mortem. Cases have been reported since 1932 by Kuhlmann,[9] Hastings,[6] Silvestrini,[14] Kejlson and Aronson,[8] Sargnon and Levrat,[13] Mardersteig[10] and Brunetti[2] (a total of 7); we are not certain that all of these cases were recognized during life, but, assuming that they were, they may be added to the following which were so diagnosed. One case each by Blackford et al,[1] by Jenkinson,[7] by Sprague et al,[16] by Fray[4] and 2 cases by Friedman.[5] Therefore, there have been only approximately 13 cases diagnosed during life. The cases reported by Friedman did not apparently have any symptoms from the anomaly; however, Friedman does not mention whether or not the arch was retroesophageal in position; indeed, one of his illustrations (Fig. 7) suggests that it was pre-esophageal in location. Renander[12] reported an interesting case in 1926, illustrating his article with photographs of remarkable plaster models which show the exact topography of the various mediastinal structures.

REPORT OF CASES

CASE 1. A. G., male, aged sixty-two, carpenter, American, complained of dyspnea on exertion for one month and loss of weight, 15 pounds in six months. (Kindly referred by Doctor W. W. Newman.) Has had attacks of nocturnal asthma for several years, is awakened by a paroxysm of coughing, after which he brings up some frothy sputum; when the paroxysm subsides he can sleep again. Moderate dysphagia of gradual onset. Moderate pain in the lower portion of the chest, attributed to coughing. A diagnosis of pulmonary tuberculosis had been made twelve years previously and no cardiac abnormality was noted at that time; a film, made at that time, at the University of California Hospital, was unfortunately destroyed by a fire some years later.

Family History. Married; 2 children; father dead of "heart disease"; mother dead of "rheumatic fever."

Physical Examination (Dr. Newman, June 10, 1932). Uninteresting, except for a slight systolic murmur at the apex and extrasystoles. No edema or cyanosis. Temperature 99.4° F. Pulse 84. Blood pressure 104/66, the same on both sides. Respiration 26. No physical findings of note. Left leg amputated below the knee as a result of a railroad accident fifty-four years ago. Sputum negative for tubercle bacilli. Basal metabolic rate normal. Electrocardiograms showed borderline right axis deviation. Blood count normal. Urine normal.

Roentgen examination of the chest shows a circular upper mediastinal tumor, about 4.5 cm. in diameter, apparently non-pulsatile, retroesophageal in position and indenting the esophagus from the left. No esophageal infil-

tration. No bone changes. Aortic knob "flattened" or hypoplastic.

Bronchoscopic Examination (Dr. L. Eloesser, August 22, 1932). Tumor indenting left tracheal wall, showing pulsation, apparently transmitted pulsation.

Impression. We believed the most likely interpretation was a circumscribed mediastinal tumor or cyst, possibly a lymphoblastoma. Dr. R. R. Newell, in consultation, suggested an upper mediastinal tumor, possibly a retroesophageal thyroid. Dr. Eloesser also believed it was a mediastinal tumor, the possibilities including "benign chondroma, cyst, dermoid or aberrant thyroid."

Treatment. Under a tentative diagnosis of possible mediastinal lymphatoid tumor, the patient was given a short course of high voltage roentgen therapy—200 kv.; filter 0.5 mm. copper plus 1.0 mm. aluminum; 33 cm. diameter skin field; 70 cm. skin-target distance; a total dose of 660 r (measured in air) anteriorly and posteriorly to the upper thorax in ten days (June 10 to June 20, 1932). Allowing for scattering and the location of the tumor, the estimated tumor dose was approximately 1,000 r.

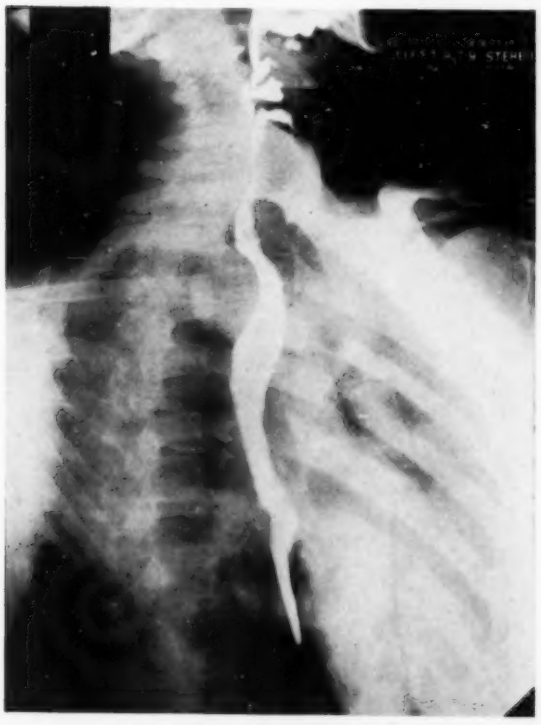

Fig. 5. Case 1. Highr ight-sided aortic arch. Left anterior oblique film. Observe the *high*, retroesophageal location of the aortic arch.

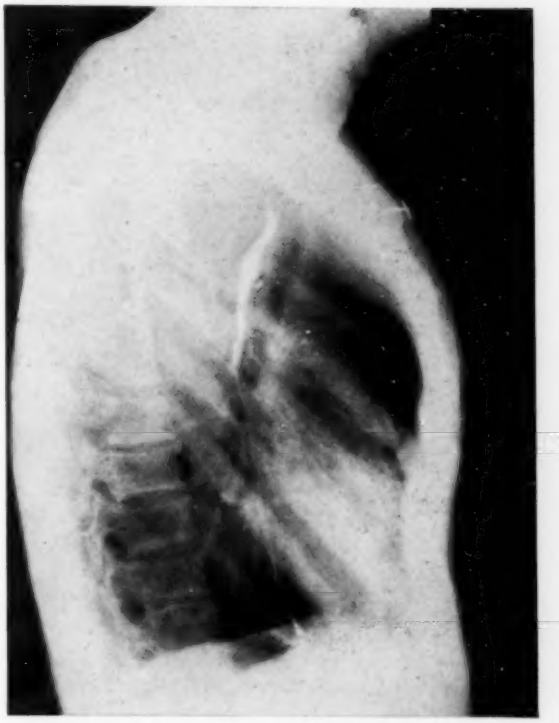

Fig. 6. Case 1. High right-sided aortic arch. Left lateral film. Observe the forward displacement of the esophagus caused by the posteriorly located aortic arch. (Note: the wire suture in the cephalic end of the sternum is an incidental unimportant finding.)

Course. No relief followed roentgen therapy, so an operation was decided upon.

Operation (Dr. Eloesser, August 23, 1932). Upper anterior longitudinal mediastinotomy under local anesthesia through modified Sauerbruch incision. Exploration revealed a large pulsating vessel lying to the left of and behind the esophagus, the latter being identified by passing a large stomach tube. A small piece of wire was inserted at the point where the vessel lay and against the trachea. The incision was closed up immediately. The patient ate his dinner that night and left the hospital in one week.

He felt better following this "decompression" but returned after five months complaining of his original symptoms. In May, 1933, he complained that his left collar bone "clicks and grinds and is painful." Apparently the piece of sternum attached to the left clavicle (subsequent to surgical division of the sternum) slips and grates on a false joint with the manubrium. There is no hernia through the left second costal cartilage defect. The patient was last seen

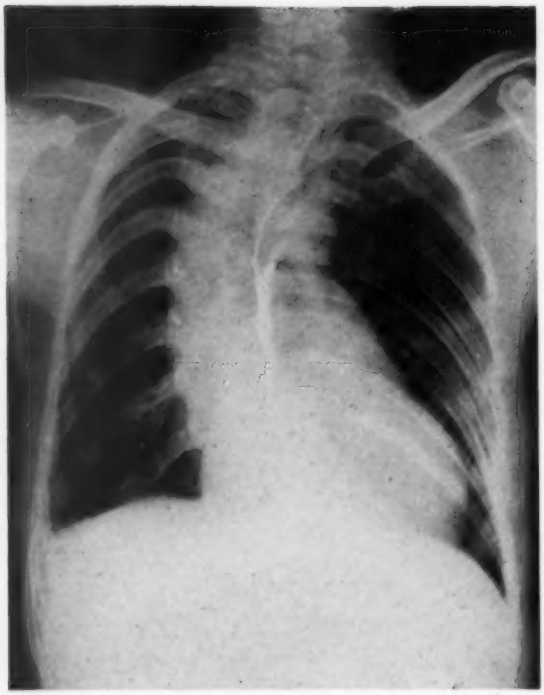

FIG. 7. Case II. Right-sided aortic arch. Posteroanterior film. Owing to the marked congenital scoliokyphosis present in this case, the upper mediastinal shadows are confusing and the diagnosis is really made from the left anterior oblique projection (see Fig. 8).

on June 12, 1934, at which time he also had some pain in the right shoulder.

Summary. An elderly male complaining of dyspnea of gradual onset, with moderate dysphagia and marked weight loss. History somewhat suggestive of carcinoma of the esophagus. Received roentgen therapy for possible mediastinal lymphoblastoma without relief. Operation showed an anomalously located aorta. According to some authorities, persistent right-sided aortic arch usually occurs as an isolated malformation and usually has no clinical significance; however, esophageal constriction is occasionally found and very rarely tracheal constriction. The case herewith reported is one of these latter types of right-sided retroesophageal aortic arch with tracheal compression and dyspnea. We assume that symptoms developed in this case because of senile ectasis and elongation of the arch, which thereby pressed on a previously unembarrassed trachea and esophagus.

CASE II. J. T., male, aged forty-seven, Italian mechanic, complained of pain and tenderness in the left costovertebral region for two months, of loss of about 40 pounds in weight and of chills. (He had no symptoms referable to the subsequently discovered aortic anomaly.)

Family History. Unessential.

Physical Examination. Marked asymmetry of the thorax apparently due to congenital thoracic scoliokyphosis. Moderate cardiac enlargement. Harsh and loud blowing murmur, of maximum intensity of the apex. Temperature 101° F. Pulse 116. Blood pressure 120/80. Blood Wassermann negative; Kahn triple positive. Electrocardiograms showed changes indicative of mild myocardial damage (Dr. J. M. Read). Multiple cutaneous petechiae developed shortly after admission to the hospital. Blood culture positive for *Streptococcus viridans*.

Roentgen examination of the chest shows marked deformity of the thoracic cage with severe scoliokyphosis. The cardiovascular outline is disturbed by this profound bony deformity. Examination of the esophagus with barium paste reveals that the aortic arch is retroesophageal in position, indenting the esophagus

FIG. 8. Case II. Right-sided aortic arch. Left anterior oblique projection. The retroesophageal position of the aorta is clearly seen. It is to be noted that this is not a case of *high* right-sided arch.

from the left. No bone changes suggestive of coarctation of the aorta.

Impression. Subacute bacterial endocarditis. Asymptomatic right-sided retroesophageal aorta.

Course. Steadily downhill. No post-mortem examination of upper thorax.

SUMMARY

Two cases of persistent right-sided aortic arch are reported, bringing the total number of cases recorded in the literature up to approximately 115 and the total number of cases correctly diagnosed in vivo to approximately 15.* One of these cases was correctly diagnosed only after surgical exploration; the other was diagnosed from the roentgen examination alone.

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* Since completion of this paper in May, 1936, Spencer and Dresser[15] have reported 3 additional cases of right-sided aorta, 2 of which had been erroneously diagnosed as mediastinal lymphatoid tumor; the third was virtually asymptomatic.

DEVELOPMENTAL AND LIFE CYCLES OF THORACIC AORTIC ANEURYSMS*

By EUGENE FREEDMAN, M.D., CHARLES S. HIGLEY, M.D., *and* HARRY HAUSER, M.D.
CLEVELAND, OHIO

WHILE aneurysms of the aorta are looked upon as a common finding among general medical patients, only 150 proved cases were found among the 163,000 patients admitted to the Cleveland City Hospital from 1922 to 1936. An analysis of these cases revealed that the majority (103, or 68 per cent) occurred in the fourth and fifth decades of life; 130 cases were in males and 20 in females. The etiologic factor in 137 cases was syphilis and in 13 arteriosclerosis.

The location of the aneurysm was found to be in the various portions of the thoracic aorta as follows: ascending portion 79, transverse portion 35, descending portion 29, and diffuse 7. According to Boyd's[1] statistics, based on a study of 4,000 cases, the great majority of patients die within two years after the discovery of the disease. It was found in this study that 40 patients (26.6 per cent) died within the first six months, 16 (11.3 per cent) within the second six months and 70 (46 per cent) died within two years. Eighty-one of the cases were proved by autopsy.

The time interval which is necessary for the development of an aneurysm is not well known, for when the patient appears for examination, the lesion is already partially developed. Experience, however, has shown that in exceptional cases when the condition is diagnosed during the early stages of luetic aortitis, in which the patient receives antiluetic treatment and in whom later an aneurysm develops, this change occurs slowly during the course of many months or years.

We have observed 2 cases of saccular luetic aneurysm of the thoracic aorta, the first of which demonstrates the possible rapidity of the developmental cycle of an aneurysm, and the second demonstrates the possible long life-cycle of a fully developed aneurysm.

REPORT OF CASES

CASE 1. F. S., colored male, aged forty-two, was admitted to the Cleveland City Hospital February 28, 1935, complaining of retrosternal pain, increasing shortness of breath and hoarseness. The symptoms began ten months prior to admission at which time he had a severe cold associated with hemoptysis and loss of weight. He was seen at that time in the Out-Patient Department. Roentgen examination of the chest revealed consolidation in the right middle lobe which was thought to be due to tumor or unresolved pneumonia. The hemoptysis ceased and the only symptom which remained was shortness of breath. The pain began one month prior to admission and was not aggravated by respiration. He returned to the Out-Patient Department on February 7, 1935, again complaining of retrosternal pain. Roentgen examination at that time showed the shadow on the right to have disappeared. A large mediastinal shadow was noticed on the left side which displaced the trachea to the right and measured 6 cm. in diameter. The blood Wassermann reaction was positive. Clinical examination revealed no definite abnormalities except for hoarseness and paroxysmal nocturnal dyspnea.

Roentgen observations of the chest on May 2, 1934, showed a dense haziness extending from the lower portion of the right hilum towards the lateral chest wall. The upper border of the shadow was sharply defined and its lower border was irregular. The vertical dimension of this shadow measured 5 cm. There was also mottling throughout the medial portion of the right base. The changes were suggestive of either an unresolved pneumonia or a lung abscess. The aorta appeared to be of normal size (Fig. 1).

Examination on February 7, 1935, showed the character of the shadow near the right

* From the Departments of Roentgenology and Medicine, Cleveland City Hospital, the University Hospitals and Western Reserve University, Cleveland, Ohio. Presented at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

hilum to have changed (Fig. 2). It was more sharply circumscribed, somewhat circular in shape, and slightly lobulated. It was smaller than previously noted and measured about 5 cm. in diameter. There was a widening of the upper left mediastinal shadow, its lateral contour extending for a distance of about 5.5 cm. from the midline. A neoplasm in the right descending bronchus was considered a diagnostic possibility, with the enlargement of the upper mediastinum being due to metastatic nodes.

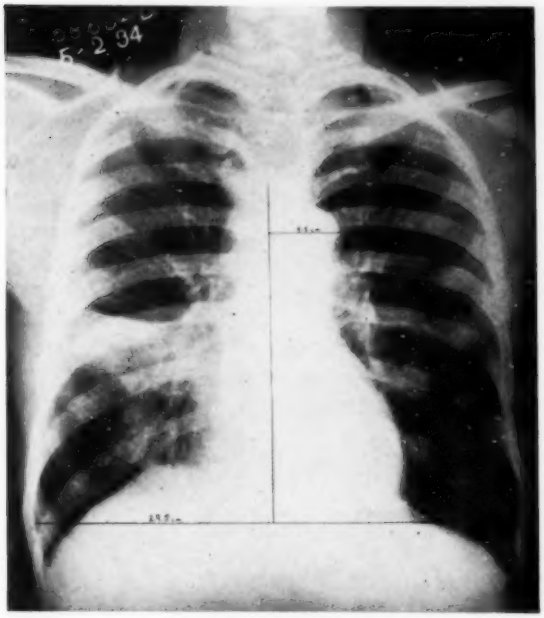

Fig. 1. Case 1. Posteroanterior view of chest May 2, 1934, showing consolidation in middle third of right lung. Mediastinal shadow of normal width.

Iodized oil was instilled into the right bronchial tree on February 23, 1935, and the subsequent film (Fig. 3) showed a normal bronchial pattern, excluding the presence of a lung tumor. The left upper mediastinal shadow appeared to have increased 1 cm. in width in sixteen days. The area of widening was less dense than the shadow of the aorta lying medial to it and its lateral contour showed a definite convexity which was sharp in outline. Roentgenoscopically, the pulsations were increased in amplitude. A left lateral view of the chest taken on March 1, 1935, showed the structure to be situated in the anterior mediastinum, to be contiguous with the superoanterior margin of the transverse portion of the aorta and to be globular in shape (Fig. 4).

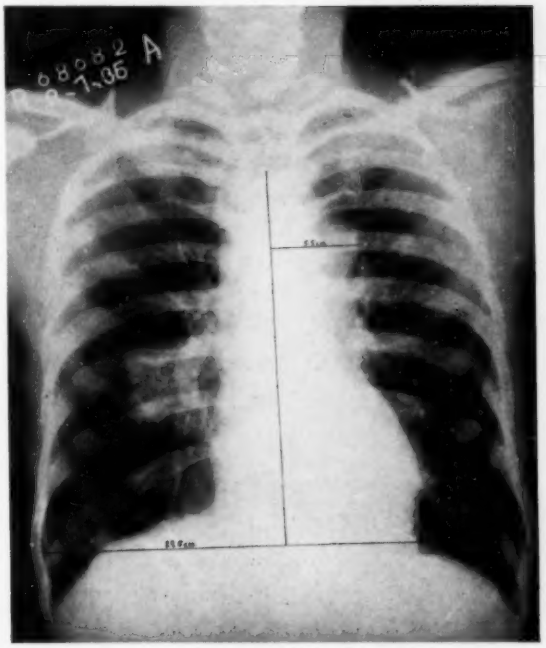

Fig. 2. Case 1. Roentgenogram of chest February 7, 1935, showing increase in size of upper left mediastinal shadow. Mass in right hilum decreased in size.

On April 6, 1935, the upper mediastinal shadow was found to extend over a distance of 8.5 cm. from the midline. The area of consolidation at the right hilum was further decreased in size (Fig. 5).

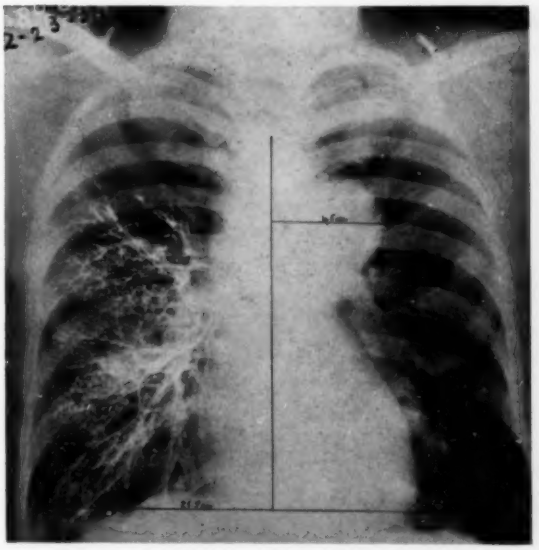

Fig. 3. Case 1. Further increase in size of mass in upper left mediastinum on February 23, 1935.

FIG. 4. Case I. Lateral view of chest on March 1, 1935, showing globular mass situated in anterior mediastinum and contiguous with aorta.

A diagnostic puncture was made of the mass with an 18-gauge needle on April 18, 1935. A pulsation was detected which was synchronous with the heart beat and free blood was obtained. With the preoperative diagnosis of an aortic aneurysm, a filigalvano-puncture was done on May 7, 1935.

A posteroanterior view of the chest taken on May 10, 1935, showed further increase in the size of the mediastinal shadow which contained the coiled gold wire previously inserted at operation.

Case II. W. D., colored laborer, aged fifty-six, was admitted to Cleveland City Hospital in November 1924, complaining of shortness of breath and pain in the back of four days' duration. Six months prior to admission he had experienced a slight throbbing pain in the midportion of his back which did not incapacitate him. He stated that at the age of twenty-eight he had a penile chancre which was not treated by specific medication.

Physical examination at that time revealed an increase in the retrosternal dullness and a tracheal tug. The blood Wassermann reaction was positive. A diagnosis of syphilitic aneurysm of the aorta was made clinically and was confirmed by roentgen examination.

During 1925, the patient received a course of antiluetic therapy consisting of mercury rubs, neoarsphenamine and potassium iodide with no subjective improvement. The Wassermann reaction, however, subsequently became negative.

Course. During the following years the patient developed a gradually increasing kyphosis and progressing dyspnea and pain. It was necessary to give him large doses of morphine sulphate daily to alleviate pain and dyspnea. There were frequent paroxysmal attacks of cough which could be relieved by hyperflexion of the spine. Prior to his death he was readmitted to City Hospital five times and spent 65 out of the 101 months of this period in the hospital. During the time he was not in the hospital he was seen at frequent intervals in the Out-Patient Department. The last and sixth admission to the hospital was on December 6, 1932, because of increasing pain and weakness. The patient had a marked kyphosis and walked with the aid of a cane. The pupils reacted to light and accommodation. The veins of the neck showed increased pulsation. There was a palpable systolic thrill over the entire precor-

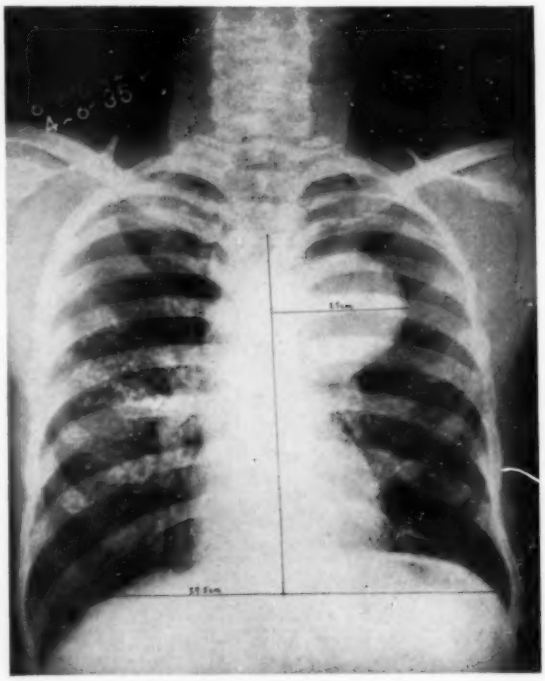

FIG. 5. Case I. Mass in upper left mediastinum extends 8.5 cm. from midline on April 6, 1935.

dium and a systolic and diastolic murmur could be heard. The blood pressure was 120/80.

Neurological examination showed sensory disturbances from the sixth to ninth thoracic levels. The zones below and above these levels were extremely sensitive. In the involved area there was anesthesia to touch, pain, heat and cold.

The patient's course was slow, but steadily downhill. About two weeks before death he developed tachycardia and reduction in pulse volume. The patient became unconscious a few days before death and died without regaining consciousness on April 4, 1933.

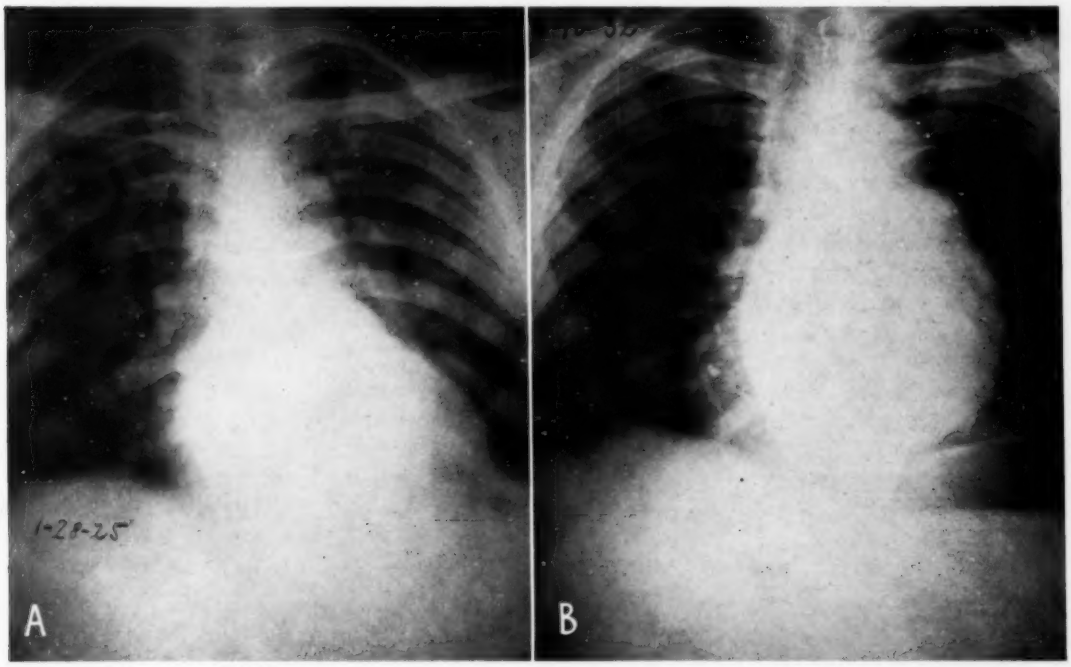

FIG. 6. Case 11. Posteroanterior views taken (*A*) on January 28, 1925 and (*B*) on June 10, 1932, showing the retrocardiac aneurysm and its increase in size during an interval of seven and a half years.

Roentgen Observations, January 28, 1925 (Fig. 6*A*). There was a moderate enlargement of the transverse diameter of the cardiac shadow, chiefly in the left ventricular region. In the center of the heart shadow a denser, oval shadow measuring about 12 cm. in length and 8 cm. in width could be seen. The left posteroanterior oblique view showed this shadow to represent a large aneurysm in the middle third of the descending portion of the arch of the aorta (Fig. 7*A*). Subsequent films taken approximately at yearly intervals showed a gradual increase in the size of the aneurysm which eventually became quite prominent and formed the left upper border of the heart shadow (Fig. 6*B*). The aneurysm failed to show pulsations at any of the roentgenoscopic examinations.

The serial left posteroanterior oblique views also showed a gradual increase in the size of the aneurysm (Figs. 7*A* and 7*B*). While in the early stages of the disease the aneurysm was of approximately the same size as the heart, later it became considerably larger. Serial lateral views of the thoracic vertebrae showed a gradual increase of bone destruction (Figs. 8*A* and 8*B*). On January 28, 1925, there was a slight erosion of the anterior borders of the bodies of the eighth, ninth and eleventh thoracic vertebrae. There was no kyphosis.

Lateral view of the thoracic spine taken on September 12, 1932 (Fig. 8*B*) showed erosion of the anterior portions of the sixth to twelfth dorsal vertebrae. The seventh, eighth and ninth dorsal vertebral bodies were most markedly involved, almost two-thirds of the anterior portion of the eighth and ninth being destroyed. The kyphosis was more marked, but there was neither gibbus nor collapse of the vertebral bodies.

The autopsy was performed by Dr. T. M.

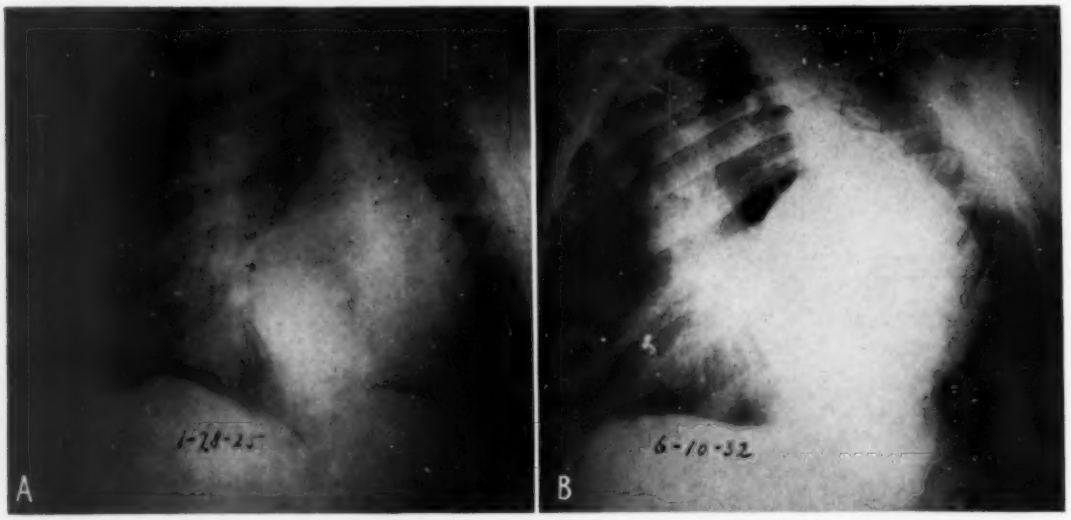

FIG. 7. Case 11. Second oblique view of chest showing the dumbbell configuration of the heart and aneurysm. The aneurysm is posterior to the heart; *B* was taken seven and a half years after the first examination.

Wille the day following death. The heart weighed 280 grams. The aortic leaflets appeared normal. The coronary vessels were moderately thickened, but patent throughout.

The aorta measured 6.25 cm. in circumference at the base and 8 cm. at the arch. There was a pouch-like dilatation in the first portion of the innominate artery measuring 3 cm. in diameter. At a distance of 17 cm. from the aortic leaflets there was a saccular dilatation of the descending portion of the arch of the aorta which measured 16 cm. in length, 12 cm. in

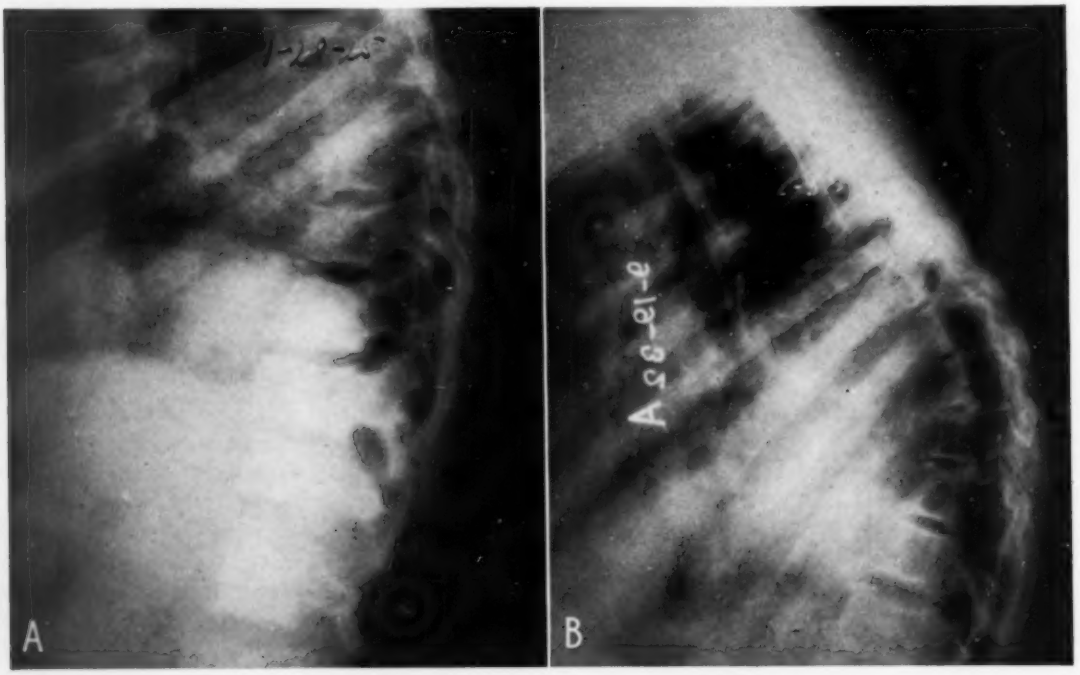

FIG. 8. Case 11. *A* shows a slight concave erosion of the anterior borders of the 7th to 11th dorsal vertebrae; *B*, taken seven years, eight months later, shows the erosion of the vertebral bodies to have increased considerably. There is a marked kyphosis.

depth and 13 cm. in width. Almost the entire sac was filled with a laminated thrombus, leaving free only a narrow lumen in the anterior portion. The sac was partly embedded in the fourth to ninth dorsal vertebral bodies, the anterior portions of which were markedly destroyed. The aneurysm was so densely adherent to the vertebral bodies that it could not be separated from them (Fig. 9).

The brain weighed 1,300 grams. The meninges were moderately distended with slightly cloudy fluid. Over the dorsal cerebellar surface there were several areas covered by a soft exudate. Microscopically these showed diffuse lymphocytic infiltration, congestion of the vessels and a large number of tubercle bacilli. The cord showed no areas of hemorrhage or necrosis. The lungs and other internal organs showed miliary tuberculosis.

Fig. 9. Case II. Photograph of the resected vertebrae into which the aortic aneurysm is embedded. A large laminated thrombus is situated in the aneurysm.

DISCUSSION

The first case had several puzzling clinical features. The patient had a consolidating lesion in the right lung, which in retrospect was most likely due to a slowly resolving pneumonic process. He was lost to observation for nine months, at which time the consolidation became smaller in size, but the upper left mediastinal shadow was seen to be moderately enlarged. During the next two months the mediastinal shadow gradually became larger. Despite its close proximity to the aorta and the increased amplitude of pulsations, the rapid growth suggested a mediastinal neoplasm rather than an aortic aneurysm. An attempted aspiration biopsy of this mass revealed the true nature of the lesion.

The remarkable features in the second case were the unusually long life-cycle of the aneurysm and the marked destruction of the dorsal vertebral bodies. Despite the fact that the seventh and eighth dorsal vertebrae were almost completely destroyed, the patient was able to walk in a flexed position. The diseased part did not form a gibbus and the remaining parts of the destroyed vertebrae did not collapse. In tuberculous or pyogenic infection or metastatic tumors, even though the destruction of the vertebral bodies is less marked than in this instance, collapse and gibbus formation are the usual sequence of events.

Schanz[2] called attention to the fact that the decrease of weight carrying strength in aneurysmal destruction of the vertebrae is partly substituted for by the aneurysm itself, which, being filled with blood under normal or abnormally high pressure and being at least partly adherent to the vertebrae, becomes a supporting organ of the vertebral column. This theory was well confirmed in our case also, since without this factor it is doubtful if the destroyed vertebral bodies could have withstood the weight of the upper trunk and head. The large, organized thrombus in the posterior portion of the aneurysm may have been also of additional support.

Another feature of this case is that death was not caused directly by either the aneurysm or by its pressure on the neighbor-

ing organs, but was due to an intercurrent disease, a generalized miliary tuberculosis.

CONCLUSIONS

1. A saccular aortic aneurysm may develop in the course of a few weeks and by its rapid increase may suggest the presence of a malignant mediastinal neoplasm.

2. A period of survival of almost ten years is not incompatible with a large aortic aneurysm with extensive vertebral erosion.

3. Although thoracic aneurysms may destroy adjacent vertebrae, they may furnish partial support for the vertebral column.

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Vol. 39, No. 5

MYELOGRAPHY WITH THOROTRAST AND SUBSEQUENT REMOVAL BY FORCED DRAINAGE: AN EXPERIMENTAL STUDY

PRELIMINARY REPORT

By W. A. NOSIK,* M.D., *and* O. A. MORTENSEN, M.D.
From the Departments of Neuropsychiatry and Anatomy, University of Wisconsin
MADISON, WISCONSIN

MANY attempts have been made to visualize disease processes in and around the spinal cord especially in those cases where clinical manifestations are few or difficult to interpret. The opaque oils have been employed most often for this purpose, particularly since the work of Sicard and Forestier,[16] and Frazier and Glaser.[3] Two objections have constantly attended the use of oil in the spinal subarachnoid space: (1) The oil is not miscible with cerebrospinal fluid and is therefore not uniformly distributed through the space. It retains its identity frequently in rather large droplets that may be arrested in areas which are not the seat of pathology. This irregularity of distribution makes it impossible to obtain a uniform and complete visualization of the space so desirable in the search for the earliest structural changes. (2) The oil remains indefinitely unless removed by operation, and its continued presence may give rise to unpleasant symptoms of root irritation. Attempts to remove the oil by puncture via the sacral canal are generally unsuccessful.† The use of opaque oils as a diagnostic aid is therefore largely limited to those cases in which subsequent laminectomy is contemplated.

Thorotrast, a radiopaque aqueous suspension of thorium dioxide, has been introduced relatively recently and used, both experimentally and clinically, for roentgen visualization of the liver and spleen, the blood vessels, and to a more limited extent to visualize the brain ventricles and subarachnoid spaces (Radovici and Meller,[8-12] Wustmann,[18] Freeman, Schoenfeld and Moore,[4] Schoenfeld and Freeman,[14] Coe, Otell and Hedley,[2] and others). It apparently possesses certain distinct advantages over the opaque oils in that it is miscible with the cerebrospinal fluid and that in the proper concentration and distribution it produces a uniform, complete visualization of the subarachnoid space. In addition it occurred to us that much of the thorotrast might be removed after the diagnostic films were taken, by forced drainage of the cerebrospinal fluid using the method suggested by Kubie and Retan.[5] Accordingly, the following experiment was performed.

EXPERIMENTAL METHOD

Dogs and monkeys were employed as the experimental animals. After preliminary medication with morphine, the animals were anesthetized with sodium amytal and placed on an inclined plane in a 30 degree tail-down position. A cisternal puncture was made and the cerebrospinal fluid allowed to escape until spontaneous flow ceased (40–60 drops). One to four cubic centimeters of thorotrast (relative to the size of the animal) was slowly injected into the subarachnoid space, the bevel of the needle directed caudally. The angle of incline was then raised to about 45 degrees and the animal placed for successive five-minute periods on its dorsal, lateral sides and on the ventral side, to insure uniform distribution of the thorotrast. Roentgenograms of the entire vertebral column were then made in the lateral and anteroposterior positions. If the films revealed a uniform and complete filling of the spinal subarachnoid space (Figs. 1, 2 and 4), the animal was immediately subjected to forced cerebrospinal fluid drainage as follows. The cisternal needle was reinserted and, depending upon the size and condition of the animal, 250–1,000 cc. of a warmed half-normal (0.45 per cent) saline solution were in-

* Now at Cleveland Clinic, Cleveland, Ohio.

† Personal communication of Dr. H. H. Reese.

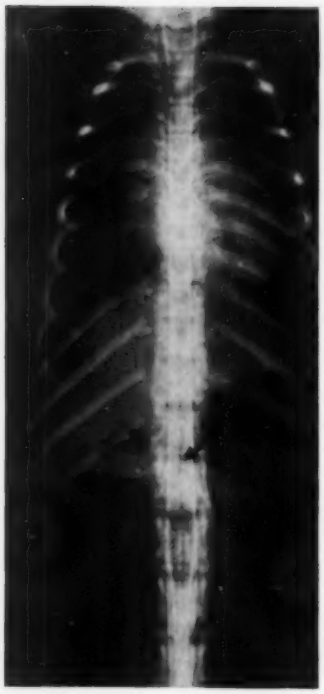

FIG. 1. Spinal subarachnoid space of monkey as outlined by 2 cc. thorotrast. Note the vessel indicated by the arrow.

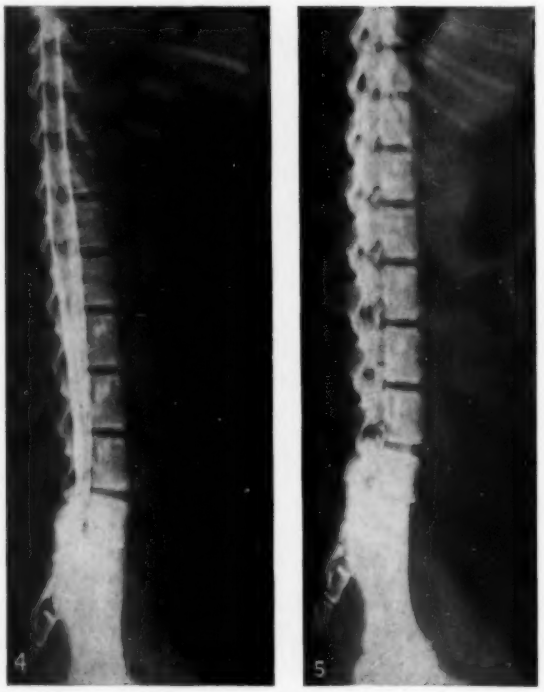

FIG. 4. Visualization of lumbar canal and caudal sac of a dog with 2 cc. thorotrast, before drainage.
FIG. 5. Same animal after forced drainage of spinal subarachnoid space.

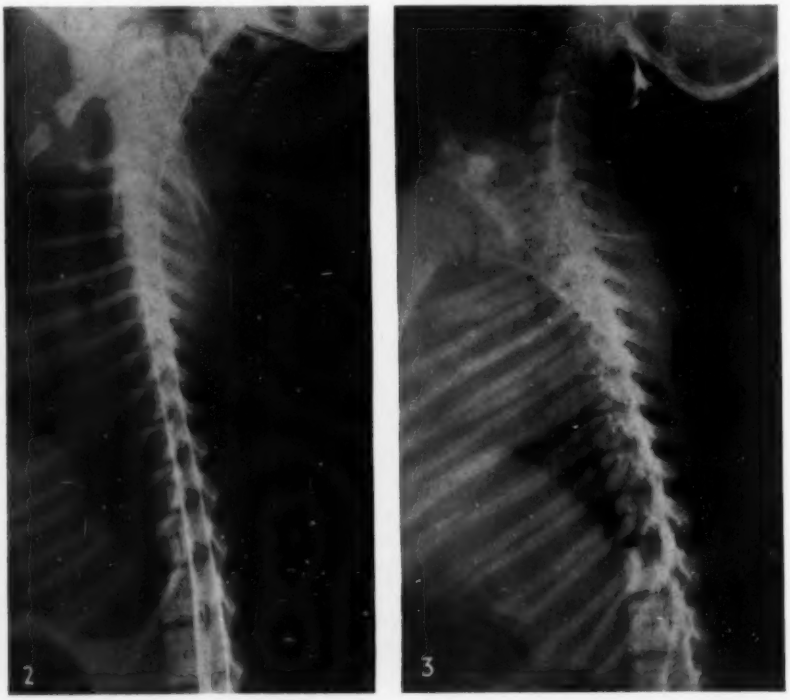

FIG. 2. Before drainage of spinal subarachnoid space with 2 cc. thorotrast as contrast medium (monkey).
FIG. 3. Same animal after forced drainage of spinal subarachnoid space. Arrow indicates backflow of thorotrast from cisternal puncture.

jected intravenously at a rate of 25–35 cc. per minute. Almost immediately a marked increase in flow from the cisternal needle was apparent. About an hour after the intravenous injection was completed the flow from the cistern had practically ceased. The needle was then removed and the second set of roentgenograms made to visualize the degree of removal of the thorotrast (Figs. 3 and 5).

DISCUSSION

It is obviously desirable to remove a foreign substance which has been introduced into the body as a diagnostic aid after it has served that purpose. This is particularly true for substances introduced into or around the central nervous system because their continued presence may give rise to unpleasant symptoms and results. These considerations, combined with the apparent advantages of a miscible opaque medium, prompted the experiment described. Not all of the thorotrast introduced is removed by this method but enough of it is to alter markedly the postoperative condition of the animal. If thorotrast is introduced without subsequent drainage, symptoms of meningeal irritation (rigidity and extension of the spine in the monkey) appear after twenty-four hours and persist for two or three days. These signs of irritation are not present in animals that have been drained subsequent to the injection of thorotrast. Both groups manifest general malaise for a few days but usually recover completely.

Forced cerebrospinal fluid drainage by the introduction of hypotonic saline solution intravenously is recognized clinically as a relatively safe method of irrigation of the subarachnoid space (Kubie and Retan,[5] Reese and Shulak[13]) and is employed in this procedure purely for the mobilization and mechanical removal of the thorotrast.

The ability to control the spread of thorotrast by gravity, and therefore through the posture of the animal, was striking. Occasionally the films revealed incomplete filling of the caudal portion of the space. Tilting the animal into the proper position readily displaced thorotrast into the most caudal portion of the sac. It is evident that the spinal subarachnoid can readily be visualized and drained without appreciable amounts of thorotrast entering the cranial cavity.

Whether or not this partial removal of the thorotrast by forced drainage will reduce the meningeal reaction in man to the extent of practical application awaits the the results of clinical trial. It would appear from this experimental study that thorotrast, if subsequently removed by forced drainage, may be the material of choice for roentgenographic visualization of the spinal subarachnoid space.

A few clinical trials in our hands would appear to justify further study of this method; for with as small an amount as 4 cc. of thorotrast, the lumbar canal and caudal sac was well visualized in one patient. Subsequent drainage revealed a quantitative return of over 89 per cent of the injected thorium dioxide.* The clinical course was much like that of the experimental animal, in showing only a short period of malaise after drainage, with no alteration of physical signs. A very mild cellular response in the spinal fluid was noted the following day.

We acknowledge with appreciation the assistance and suggestions of Dr. H. H. Reese, Dr. W. J. Bleckwenn, and Dr. W. E. Sullivan of the University of Wisconsin, in the preparation of this experimental work, and thank Mr. Stoughton White for his technical aid.

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RUPTURE OF CONGENITAL SOLITARY KIDNEY

REPORT OF A CASE IN WHICH THE DIAGNOSIS WAS MADE DURING LIFE

By LESTER G. ERICKSEN, M.D.
SOUTH BEND, INDIANA

INTRODUCTION

THERE are numerous cases in medical practice, both published and unpublished, in which the only well-functioning kidney a patient possessed was removed surgically with a fatal result. Previous to the advent of urography this was a very common occurrence and pardonable to a large extent. However, with the addition of retrograde and, later, excretion urography to the other diagnostic procedures, these surgical catastrophies have become unpardonable. We now have a diagnostic routine which, if carried out on every patient on whom any operative procedure in reference to the kidney may be contemplated, is practically foolproof.

With a patient, in whom a traumatic rupture of a kidney has occurred, the physician is likely to allow the severity and gravity of the injury to overshadow his good judgment to such an extent that he considers immediate surgical interference before determining the presence of a well-functioning kidney on the other side. The average physician does not realize the frequency of congenital anomalies of the kidney which in routine urologic practice constitute about 40 per cent of all pathological lesions of the kidney. A congenital lack of development to the extent that it interferes with function will occur in about 1:400 autopsies, while a unilateral, poorly functioning kidney from all causes occurs very frequently. Thus one can appreciate the necessity of clinical recognition, not only for establishing a correct diagnosis, but also to assure a sound prognosis.

Among the congenital anomalies of the kidney are three borderline conditions very closely related but differentiated by Gutierrez[4] as hypoplastic kidney, renal aplasia and congenital absence of the kidney. One may question the need for an accurate differentiation and classification of these three developmental anomalies on the grounds they are merely different stages of the same developmental process, and that the outcome following surgical removal of the sound kidney is the same in all—uremic coma and death. I believe it is clinically worth while, however, to differentiate between hypoplastic kidney as one group and combine renal aplasia and congenital absence of the kidney as the other group.

EMBRYOLOGY

Embryologically, these anomalies have a common basis. Boyden[1] dissected a 10 mm. human embryo in which one kidney was in the process of disappearance. From this he reconstructed the cause of this anomaly in man. In this embryo it was found that the right wolffian duct had reached the cloaca and given rise to a ureter which, in turn, had grown in the blastema of that side and was apparently developing into a normal kidney. The left wolffian duct, however, was interrupted in its down growth and failed to reach the cloaca; thus no left ureter was developed. There was, however, a left blastema but it was not differentiating into tubules (Fig. 1).

Boyden,[1] working with chick embryos, was able to demonstrate that the blastema appeared as an anlage in spite of lesions which prevented the formation of the ureter. Brown (cited by Boyden), working with a strain of mice with inherited kidney defects, was able to show that the development of the blastema into a normal kidney was directly dependent upon the ureteric bud reaching the blastema. Any retardation of the bud in reaching the blastema resulted in various degrees of poor kidney development, ranging from no develop-

ment, in which case no ureteric bud appeared, to rudimentary or hypoplastic kidneys in which the ureter had been delayed in reaching its destination. In none of Brown's cases was there an example in which the blastema had failed to appear. The above work offers a very plausible explanation for the various degrees of underdevelopment and those cases in which a vestige of ureter remains on the side of the missing kidney. It also refutes the theory that absence of the metanephric blastema is the cause of congenital absence of the kidney.

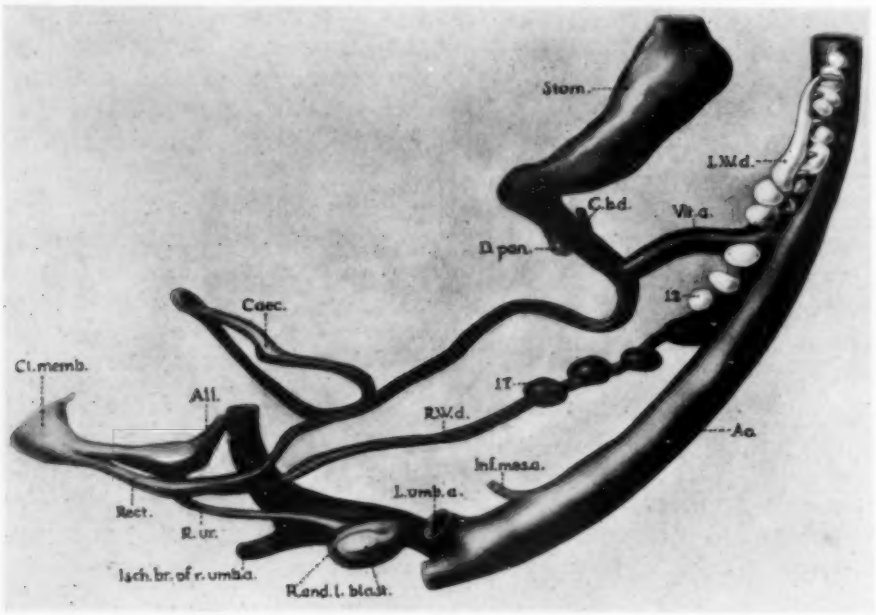

Fig. 1.* Graphic reconstruction by Boyden of 10-mm. human embryo illustrating arrested development of wolffian bodies, failure of left wolffian duct to reach cloaca, and fusion of left blastema with right kidney as latter is entering umbilical crotch. *All.*, allantois; *Ao.*, aorta; *Caec.*, caecum; *Cl. memb.*, cloacal membrane; *C.b.d.*, common bile duct; *D. pan.*, dorsal pancreas; *Inf. mes. a.*, inferior mesenteric artery; *Isch. br. of r. umb. a.*, right ischiatic artery; *L. umb. a.*, left umbilical artery; *L.W.d.*, hydronephrotic left wolffian duct; *Rect.*, rectum; *R. and l. blast.*, right and left renal blastema; *R. ur.*, right uterer; *R.W.d.*, right wolffian duct; *Stom.*, stomach; *Vit. a.*, vitelline artery; *12*, lowest glomerulus of left wolffian body; *17*, lowest glomerulus of right side.

* Reprinted by courtesy of *The Anatomical Record.*

HYPOPLASTIC KIDNEY

While the normal kidney has the capacity to undergo functional hypertrophy after removal of its mate, the hypoplastic kidney does not; the postoperative result is invariably uremic coma and death. Therein lies the danger of surgery in a patient in whom this anomaly is present, but its importance not recognized. Since it is said to occur once in 400 autopsies, the possibility of such an occurrence should always be kept in mind.

True congenital hypoplastic kidney must be differentiated from secondary atrophy due to various disease processes. In true hypoplastic kidney there has been an arrest in its development. This kidney has never been any larger than its present size which is from three to six times smaller than its mate. On a good flat film of the urinary tract, this may be readily demonstrated and should arouse immediate suspicion in the mind of the examiner. In such a case

further study by means of the cystoscope will show normal secretion of urine coming from both ureters. When the functional tests with reference to the excretion of urea and the color dyes is done, it will be found that the hypoplastic kidney will show a decrease in comparison with the opposite side should that kidney be normal. However, if the opposite side is diseased, both kidneys will show decreased function. In this case according to Gutierrez,[4] the flat film showing a difference in size and the bilateral pyelogram must be relied upon. He has described two types of hypoplastic kidney which are illustrated in the accompanying Figure 2.

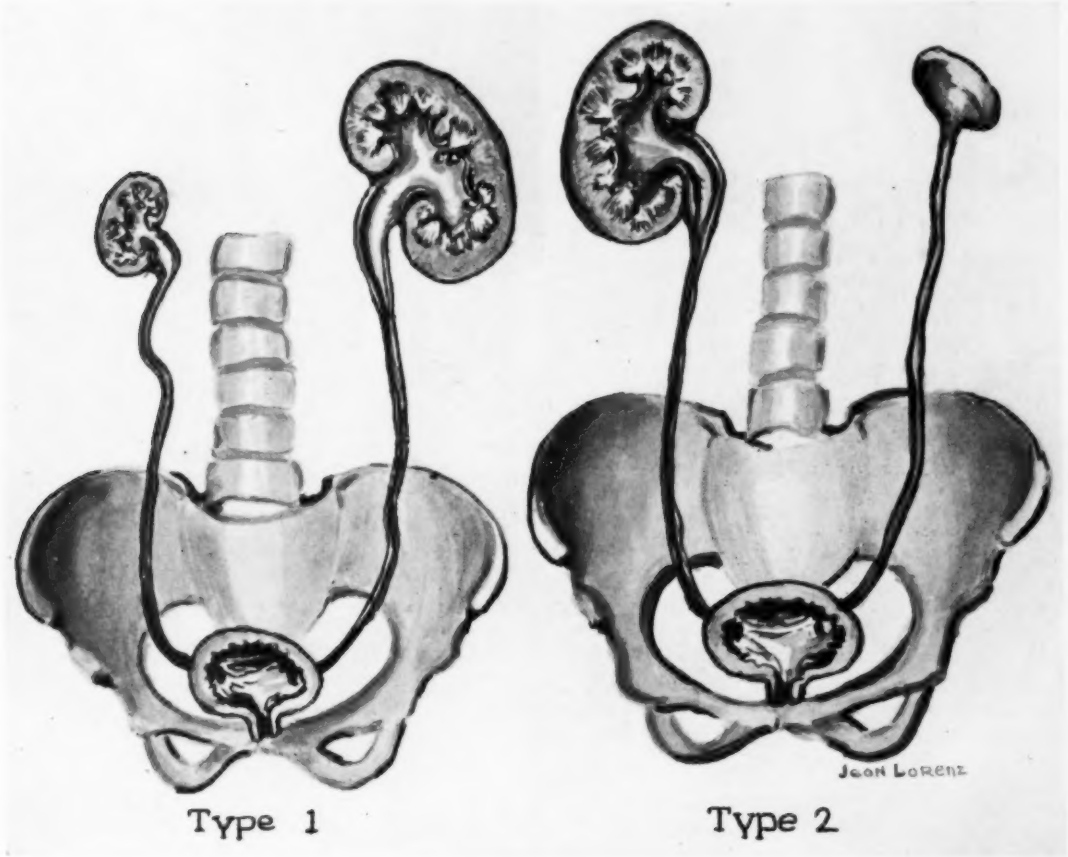

Fig. 2. Diagrammatic representation of two types of hypoplastic kidney as described by Gutierrez. Type 1. Note small right kidney with small but normal calyces and pelvis. Pelvis may be pear or bottle shaped. Type 2. Medullary portion and pyramids are absent and the pelvis is hydronephrotic.

Renal Aplasia and Congenital Absence of the Kidney

Accurate differentiation between what has been classified as unilateral renal aplasia (Fig. 3) and congenital absence of one kidney (Fig. 4) is of interest to the pathologist and the embryologist, but only of academic interest to the clinician since the differentiation can only be made at autopsy.

In both conditions cystoscopy will reveal no function on one side with partial or non-development of the ureter. Autopsy may show a small amount of non-functioning renal tissue or no vestige of kidney whatever. For practical purposes one may classify both as congenital absence of the

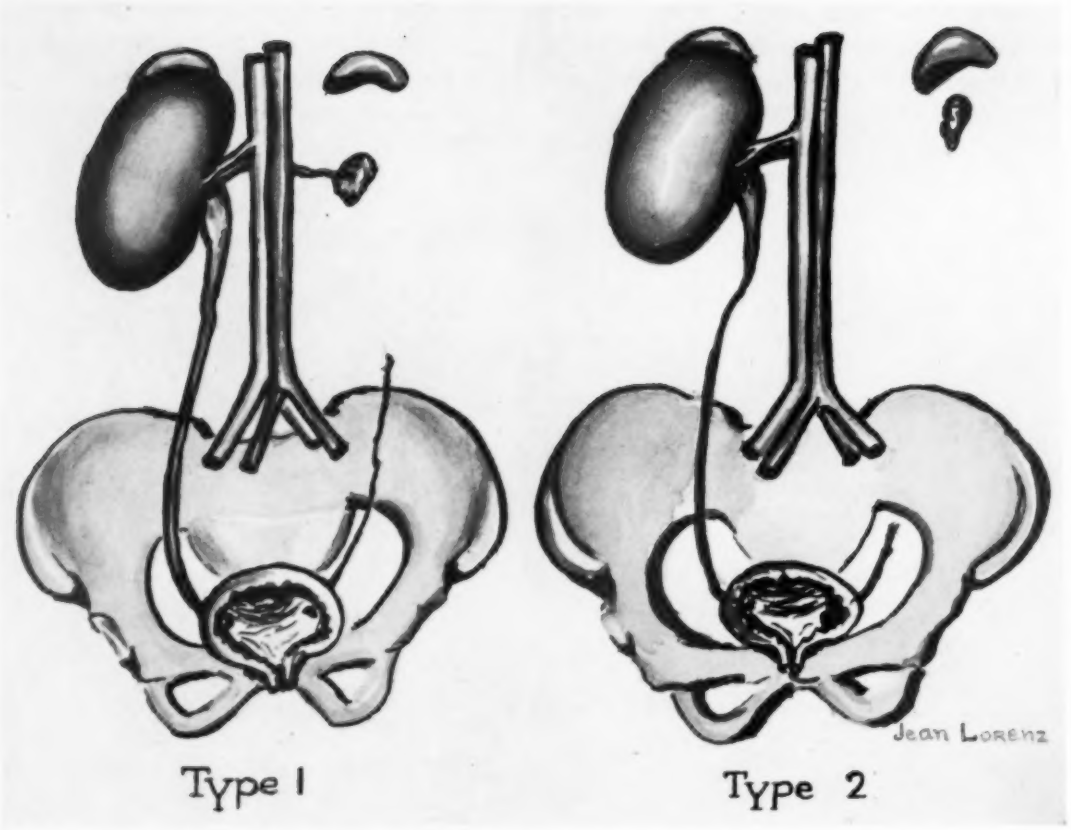

Fig. 3. Diagrammatic representation of two types of hypoplastic kidney as described by Gutierrez. Type 1. A small mass of renal tissue which has a small underdeveloped arterial connection with the aorta. Type 2. A small mass of renal tissue which has no arterial connection with the aorta whatever. Note that the ureter is underdeveloped and not patent in either case. A suprarenal gland is present in both types.

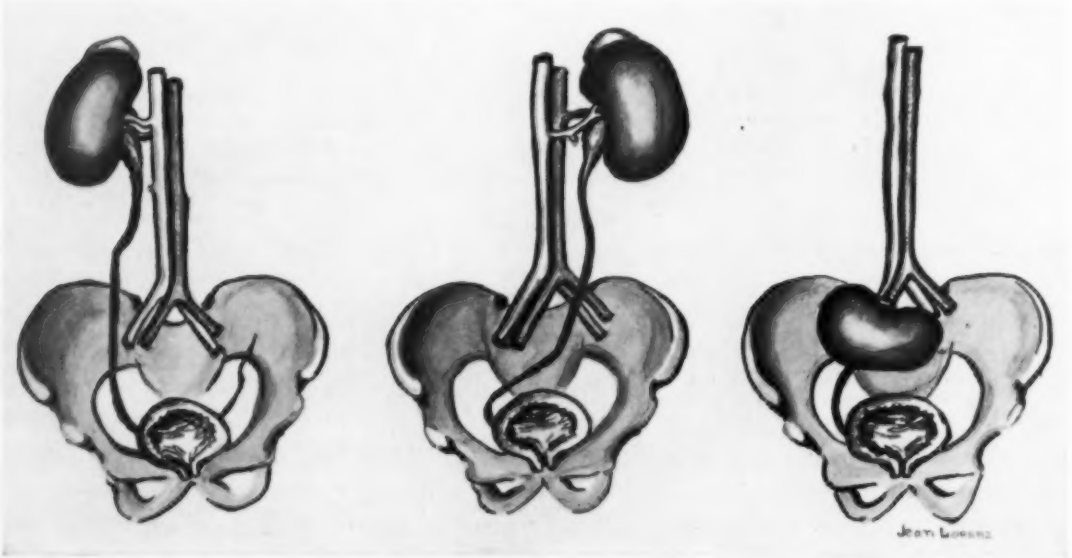

Fig. 4. Diagrammatic representation of three types of true congenital absence of one kidney as described by Gutierrez. Note absence of any mass of renal tissue whatever and also absence of suprarenal gland. There is only one ureteral opening into the bladder and one-half of the bladder trigone is missing.

kidney. A review of statistics shows this anomaly to occur more frequently on the left side than on the right and the incidence to be about 1:400 autopsies. It is to be noted in Table 1 that all of the cases here reported were left sided. No explanation can be given for this.

About 70 per cent of these cases will show accompanying congenital malformations of the genital tract. In the male this may consist of any one or a combination of the following occurring on the side of the absent kidney:

1. Rudimentary or absent seminal vesicle.
2. Rudimentary or absent vas deferens.
3. Atrophy of prostate.
4. Absence of ejaculatory duct.
5. Rudimentary or absent epididymis.
6. Atrophy or absence of testicle.
7. The rudimentary ureter ends in the seminal vesicle or in the vas.

Table I

DIGEST OF REPORTED CASES

Author and Date	Sex and Age	Occupation	Side of Kidney	Nature of Accident	Type of Treatment	Day of Death after Accident	Notes
I Melchoir (Germany) 1928	M. 27	Physician	L.	Motor accident	1. Laparotomy 2. Nephrectomy (day after accident)	Fifth	On admission general condition good. Bruising in left flank. Bladder contained pure blood. Next day worse. Anterior laparotomy showed some distention, but no intraperitoneal injury. Hemorrhage around left kidney. Wound closed. Lumbar nephrectomy. Kidney showed deep transverse cut into hilum.
II Speer (U.S.A.) 1929	M. 27	Not Stated	L.	Motor accident	Nephrectomy soon after admission	Second	Conscious on admission. Also fracture of left femur. In shock, but improved some, so nephrectomy done. Complete tear into pelvis and vein.
III Brattstrom (Sweden) 1932	F. 16	School girl	L.	Kicked by horse while bicycling	Nephrectomy soon after admission	Third	On admission bladder full of pure blood. Condition rapidly deteriorated so operation performed. Kidney found to be pulped. At autopsy no ureter or suprarenal present and uterus bifid.
IV Thompson (Ireland) 1932	M. 22	Not stated	L.	Kicked in loin at football	Nephrectomy several days after accident	Tenth day after operation	This patient watched for several days at home before persistence of pain and bleeding demanded operation. Kidney hopelessly damaged.
V Turton and Williamson (England) 1932*	M. 12	School boy	L.	Fell about 5 ft. off gate on to left flank	Drainage of retroperitoneal extravasation 11th day after accident	Eleventh	Expectant treatment at first and patient improved, but then became worse.
VI Taylor (England) 1870†	M. 22	Not stated	L.	Fell to ground from roof of building	Expectant	Second	Previous health good. On admission to hospital condition good except for pain in left flank. Bladder contained much blood. Died suddenly second day. Autopsy showed kidney torn completely across with separation of fragments. Much hemorrhage. No right kidney or ureter. No ureteral opening into bladder on right side.
VII Ericksen (U.S.A.) 1934**	M. 32	Laborer	L.	Fell about 2 ft.	Expectant with ureteral drainage	Eighth	See case report.

* The first 5 cases reported by Turton and Williamson.
† Sixth case added from literature by Ericksen.
** Seventh case reported by Ericksen.

8. Associated defects of the external genitalia such as hypospadias, non-descent of the testes, pseudo-hermaphrodism.

Associated genital defects are even more common in the female. One or a combination of the following may be found:

1. Uterine defects.
2. Absence or rudimentary development of the fallopian tube.
3. Absence or atrophy of the ovaries.
4. Vaginal defects.
5. Defects of the external genitalia.
6. Abnormal ending of the rudimentary ureter.

A helpful point in suspecting the possibility of congenital absence is that should one find a female patient with congenital malformation of the genital organs, she is practically sure also to have a congenital absence of the kidney.

Renal agenesis has been discussed since the time of Aristotle and there are numerous reports in the literature concerning this anomaly. Until recently, however, the literature on this subject was rather confusing in that the various authors failed to differentiate between atrophy of a kidney due to disease and true congenital absence, so that statistics as to the incidence are not entirely accurate. Collins,[2] in a recent paper, states the incidence of congenital absence of the kidney to be 1:920 as compiled from a review of 337,488 autopsies.

In contrast to the numerous articles on different phases of this condition, there have been reported only 6 cases of traumatic rupture of a congenital, unilateral kidney and in none of these cases was the condition diagnosed ante mortem. Turton and Williamson[6] have recently reviewed the literature and found 4 cases to which they add one of their own making a total of 5. I have been able to find one additional case reported by Taylor[5] in 1870 which, with the case here reported, makes a total of 7 (Table 1).

CASE REPORT

A male, aged thirty-two, a patient of Dr. R. R. Harris, entered the hospital the morning of April 18, 1934. At 10:00 P.M. the night previous, while about his duties as a night watchman on a construction project, he stumbled and fell against a 2″×4″ timber, the distance of the fall being about 2 feet. The patient did not think he was badly injured and was not seen by a doctor until about eight hours later at which time he complained of pain in his left flank. A roentgen examination was then made of his back and it was thought he had suffered a fracture of the left transverse process of the third lumbar vertebra.

The patient was transferred to the hospital and the entrance examination showed a well-developed, poorly nourished white male lying quietly in bed complaining of pain in the left flank. The pulse was 80, respirations 20, the temperature was normal and the blood pressure was 120/78. Important points in the physical examination were as follows: The abdomen showed a fullness over the left side and into the left flank which was dull to percussion. There was a marked rigidity and tenderness over the left abdomen and flank extending toward the right as far as the midline. The urine was light red color and contained much albumin and numerous red blood cells. The hemoglobin was 85 per cent with 3,900,000 red blood cells and 9,700 white blood cells. The patient was then sent to the roentgen department for further study and the following report was made:

"A flat film of the kidney and bladder region was taken (Fig. 5). This shows a marked gaseous distention of the bowel with the small bowel pushed toward the right and somewhat upward by a mass on the left side of the abdomen. The psoas muscle shadow on the left is obliterated while the right is well visualized. The left kidney cannot be outlined nor can the right because of the large collection of gas over the right side. The left sacroiliac joint is rather hazy while the right is very clearly defined. There is a round density about 1 cm. in diameter, overlying the left iliac fossa. The examination suggests that the mass represents a hemorrhage into the left retroperitoneal space possibly due to a ruptured kidney or severe muscle injury. There is no evidence of bone injury. A marked calcification of the pelvic vessels is shown.

"Due to the possibility of a traumatic rupture of the kidney, the patient was given neoskiodan intravenously. Films taken at fifteen

minute intervals over a period of one hour show a dilatation of the calyces of the left kidney with a definite extravasation of the opaque medium out of the kidney and into the space occupied by the mass (Fig. 6). There is a possibility that the round density previously described overlying the left ilium is a kidney stone which has fallen through the rent in the kidney into the retroperitoneal space. During the period of an hour in which films were taken it was impossible to visualize any dye in the right kidney pelvis nor was any opaque medium seen to enter the bladder (Fig. 6). Therefore, there is a question as to whether there is a functioning kidney on the right side.

"For this reason a retrograde pyelography was done and it was impossible to pass the catheter more than 2 inches up the right ureter where an obstruction was encountered (Fig. 7) The left ureter was catheterized readily, but shows the ureter to be displaced toward the midline by the mass on the left side. Opaque medium was injected into the left kidney pelvis which had decreased one-third in size, no doubt due to the free drainage following the catheterization. It was not possible to fill the right kidney due to the obstruction in the ureter. The catheter was forced out of the right ureter when an attempt was made to inject opaque medium and the ureter was visualized as a small pencil line extending only 2 inches above the bladder (Fig. 7). The supposition therefore is that the patient has a congenitally absent or non-functioning right kidney with occlusion of the ureter in its lower third.

"Conclusions: (1) non-functioning or absent right kidney; (2) traumatic injury to left kidney."

Fig. 5. Flat film of the urinary tract. Note the mass in the lower left abdomen displacing the gas-filled bowel; the obliteration of the left psoas shadow and haziness of the left sacroiliac joint. Attention is called to the small round density overlying the left ilium.

Fig. 6. Film taken forty-five minutes after the intravenous injection of diodrast. Note extravasation of the opaque medium into the left perirenal space with marked dilatation of the left kidney. No opaque medium can be seen in the right kidney but the fact that there is no opaque medium in the bladder is more important. Note that the calcified density is below and outside the left kidney. This represents a urinary stone which has fallen through the rent in the kidney.

FIG. 7. Pyelogram taken following cystoscopy and catheterization of the ureters. Note the stricture of the right ureter 2 inches above the bladder.

Following the above findings it was decided to treat the patient conservatively. The catheter was left in the kidney and good drainage was established. The patient progressed favorably until April 23, five days following the injury when the catheter slipped out and drainage stopped. At this time the blood urea nitrogen was 39.44 mg. per 100 cc. (normal 12-15 mg.), and the total non-protein nitrogen was 99.9 mg. per 100 cc. (normal 25-35 mg.). Following re-insertion of the catheter and irrigation of the kidney, his condition temporarily improved. On April 25, the left kidney ceased to function and the patient lapsed into uremic coma and died at 7:20 A.M., April 26, eight days after the injury.

Post-Mortem Findings. A post-mortem examination was done by Dr. F. P. McNamara, pathologist, whose report follows:

Necropsy Abstract (No. 220). The only important anatomic findings were in the urinary tract. A left retroperitoneal mass extended from the diaphragm downwards nearly to the inguinal canal. On dissection this was found to be due to a large amount of recently clotted and fluid blood which surrounded the left kidney. The latter was at least one and one-half times larger than normal. About the lower half of the kidney the blood was mixed with urine. After removal a renal calculus 5 mm. in diameter was found outside the capsule at the lower pole of the kidney. This was evidently the explanation of the shadow seen in all the roentgen films. On section of the kidney a ragged tear extended from a moderately dilated pelvis through the entire renal parenchyma and a torn arcuate artery was the evident source of the hemorrhage (Fig. 8). Apparently, the renal calculus had been forced through the tear and gravitated to the lower pole of the kidney. The ureter on this side was normal. The bladder was contracted, but on dissection the trigone was clearly demarcated. A probe entered the right ureter for approximately 5 cm. On further dissection, the ureter was fibrosed above this point and terminated in what appeared to be a thickened, fibrous renal pelvis (Fig. 8). Grossly, the kidney seemed to be entirely lacking, being represented by fibrosed fat. The suparenal body was also missing and no arterial connection

FIG. 8. Photograph of the pathological specimen. The left kidney is enlarged and there is a rent in the lower pole. The urinary stone can be seen lying in the blood clot below the lower pole. A fibrous mass is all that represents the right kidney. The bladder is normal.

could be demonstrated between the aorta and the mass at the upper end of the ureter. On histological examination of the latter, a few tubules resembling collecting tubules were found. However, had the origin of the tissue been unknown, it would have been impossible to identify it as renal tissue. *Anatomic Diagnosis:* (1) Congenital absence of the right kidney and adrenal; fibrous obstruction of the right ureter; hypertrophy of the left kidney; (2) traumatic rupture of the left kidney with extensive perirenal hemorrhage; extrusion of the renal calculus.

DISCUSSION

As shown by Boyden,[1] embryologically these three conditions are merely stages of the same developmental process, depending on whether the ureteral bud develops at all in which case there will be no evidence of kidney or ureter. If the bud is delayed in reaching the blastema, there will be various stages of development ranging from the small mass as shown in this case, to a hypoplastic kidney. Because of the above and because renal aplasia and congenital absence of the kidney can only be differentiated at post mortem, from a clinical standpoint these congenital malformations of the kidney can be classified into two groups—hypoplastic kidney and congenital absence of the kidney.

Perhaps the reason none of the cases of traumatic rupture of the kidney previously reported were diagnosed ante mortem is that intravenous urography was not utilized. The technique of retrograde pyelography is such that only one properly trained can use it. Also, when the retrograde method is employed in a case of trauma to the kidney, it is not without a certain amount of shock which the patient may not withstand. Excretion urography, on the other hand, requires only the intravenous injection of a medium such as diodrast to visualize the presence of a normal pelvis on one side and its absence on the other. Also, it is probable that the diagnosis of a rent in the kidney or severance of a ureter can be made. Intravenous urography is the best diagnostic aid we have in determining traumatic injuries to the urinary tract.

It is possible that the absence of a shadow of a kidney pelvis on one side may be only temporary due to reflex irritation or the shadow may be obscured by gas in the bowel. In this case the diodrast can be repeated intravenously and if there is still no evidence of a kidney pelvis on one side, the patient should be checked by cystoscopy as in the case here reported. Renal hypoplasia and congenital absence of the kidney are sufficiently frequent that the possibility of their occurrence should always be kept in mind and a preoperative diagnosis made of a well-functioning kidney on the opposite side before removing a traumatized kidney. To realize that these cases are not always properly studied preoperatively, one need only note that of the 6 cases previously reported (Table 1), none had a clinical diagnosis of single kidney and 4 of them had a nephrectomy performed.

Of these two conditions discussed above, hypoplastic kidney is the more dangerous. If a cystoscopy is done and a normal excretion of urine is seen coming from the kidney opposite to that on which surgery is contemplated, it is possible for the examiner to assume a functioning kidney to be present without going further and making the dye and blood urea nitrogen determinations. If the injured kidney is removed, it is impossible for the remaining kidney, with limited function, to sustain life. One is not so apt to make such an error if, when cystoscopy is done, only one ureteral opening can be found; or if two are found, no urine is observed coming from one of the openings. With the proper utilization of the diagnostic procedures we have at our command today, there is no excuse for removing the only functioning kidney a patient possesses.

Assuming that one has made a diagnosis of a traumatic rupture of a unilateral kidney, what then is the treatment to be used? It may be noted from Table 1, in Cases V, VI and VII, expectant treatment was tried and all three patients succumbed. In view of this fact either the injured kidney should be sutured, or, if this is not possible, some

type of plastic operation should be done. At least it would seem that the injured kidney should be explored and further treatment determined by the extent of the injury to the kidney.

CONCLUSIONS

1. The literature on traumatic rupture of a congenital solitary kidney is reviewed and to the cases reported one more is added.

2. This is the only recorded case in which an ante-mortem clinical diagnosis of traumatic rupture of a congenital solitary kidney was made.

3. The embryology of the development of congenital absence of the kidney is discussed.

4. It is suggested that inasmuch as renal aplasia and congenital absence of the kidney can only be differentiated at necropsy, the two conditions be combined and classified in the one term "congenital absence of the kidney." Thus, a clinical classification of renal hypoplasia and congenital absence of the kidney is sufficient.

5. The diagnostic points to be used in recognizing the above two conditions are given.

6. The value of intravenous urography in traumatic injuries of the urinary tract is emphasized and a diagnostic procedure outlined which is to be used in all cases where surgery on a kidney is contemplated.

7. It is suggested that all cases of trauma to a unilateral kidney should be explored and the type of treatment determined by the exploratory findings.

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CALCINOSIS UNIVERSALIS*

REPORT OF CASE WITH AUTOPSY FINDINGS

By S. E. GOULD, M.D.
ELOISE, MICHIGAN
AND
F. T. RAIFORD, M.D.
DETROIT, MICHIGAN

THE etiology of calcinosis universalis is little understood. In the present case report there were a number of interesting findings, some of which may be of etiological importance.

K. G., colored female, aged thirty-one, married, entered Trinity Hospital on August 31, 1935, complaining of weakness. Patient was always obese as a child. In February, 1934, she weighed 221 pounds and went on a reducing diet. During the month, she consumed a mixture of 1 gallon of vinegar and 1½ pounds of magnesium sulphate, after which she began to feel sluggish and listless. In April, an abscess of the right breast was incised and drained, and shortly afterward she developed furunculosis of the skin and later noticed swelling of the ankles and fingers. In October, 1934, she noticed a dark discoloration over the forehead and the presence of three hard painless "knots" under the skin, one in the right thigh, another near the umbilicus, and a third in the right flank. Since January, 1935, she has been unable to walk and since April unable to use her arms or hands. The patient is now confined to bed complaining of weakness and of generalized tenderness and pain. During the past week she has had abdominal cramps and occasional vomiting. Her present weight is about 135 pounds. Her daily temperature varies up to 100° F., the pulse from 80 to 90, and the respirations average 20. *Past History:* She injured the left side of her head in 1929. Alcohol has been used to excess, cigarettes moderately. She was told that her blood was bad and has received "blood shots." She has always had dyspeptic symptoms and constipation. She has a chronic pelvic discharge, and since January, 1935, amenorrhea. Seven years ago she suffered a "nervous breakdown." She is easily excited and has general bodily muscular pains. *Physical Examination:* Positive physical findings included the following: a scar in the right frontal area; limitation of motion of the jaws; marked collar atrophy of the skin of the neck; prominent supraclavicular pulsations; mottled depigmented areas of the skin of the face, neck and abdomen, with desquamation; kraurosis vulvae; muscular atrophy of the extremities; absence of deep reflexes of the extremities. In the region of the umbilicus cn the right flank there were a number of small hard subcutaneous masses which were freely movable and not tender. *Laboratory Findings.* Urinalysis: specific gravity, 1.026 to 1.032; albumin, negative to trace; many leukocytes. Blood Kahn test positive. Coagulation time four min. Hb., 50 per cent; red bood cells, 2,380,000 white; blood cells, 9,500; polymorphonuclears 55 per cent, lymphocytes 43 per cent, monocytes 2 per cent; non-protein nitrogen 25 mg. November 11, 1935, serum calcium 9.3 mg., plasma phosphorus 3.9 mg., October 28, 1935, phosphorus 4.3 mg., October 31, 1935, serum calcium 10.9 mg., serum phosphorus 2.9 mg., phosphatase 1.5 Bodansky units. Biopsy from hard, subcutaneous mass in the region of the right ilium showed fatty and fibrous tissue with areas of necrosis, much calcification, and some surrounding lymphocytic infiltration, and thrombosis of a few arterioles. Roentgenograms taken (Dr. J. E. Lofstrom) on September 16, 1935, showed large mottled areas of calcification in both flanks and in the lateral aspect of both thighs, with similar, less marked changes, in the medial aspect of both thighs. In many places the areas of calcification were limited to the fascial planes and had a somewhat symmetrical distribution. No definite evidence of bone change other than narrowing of the phalangeal joint spaces was seen. Treatment given included disodium hydrogen phosphate (gr. 5, t.i.d. eleven weeks), calcium lactate (gr. 15, t.i.d. nine weeks), haliver oil with viosterol, potassium iodide, mercury inunctions and exposure of the body to ultraviolet radiation. During her

* From the Departments of Pathology, Wayne University College of Medicine, Detroit, and Eloise Hospital, Eloise, Michigan, and the Department of Medicine, Trinity Hospital, Detroit.

stay in the hospital the patient was constipated, had constant pains in the legs and back and developed decubital ulcers. She left the hospital on December 2, 1935, showing slight improvement and being able to move her hands and legs. However she was readmitted April 1, 1936, and remained until April 29, during which time there was a progressive loss of weight. Her skin showed mottled areas of depigmentation and appeared glazed and leathery. Roentgenograms on April 13, 1936, showed evidence of slight cutaneous and subcutaneous calcification in the right upper arm and axilla, and in the soft tissue of the right breast; a fairly marked degree of calcification over the lower abdomen, hips and buttocks. In the latter locations there was essentially no change since the previous examination in September, 1935. There was loss of lime salts from the femora, evidence of marked subcutaneous calcification over the lower anterior aspect of the right leg and a small amount of calcification in the left leg. There was no evidence of subcutaneous calcification in the skull or hands. The joint spaces of the hands were normal but there was decrease of lime salt content in the bone. *Diagnosis:* Calcinosis universalis. On May 20, 1936, while at home, she developed marked abdominal distention and on the next day expired. Autopsy was performed nine hours later (S.E.G.).

Fig. 1. Photograph of patient at autopsy showing several subcutaneous calcareous masses.

Fig. 2. Roentgenogram showing multiple calcareous deposits.

External Appearance. The body was that of an emaciated colored female about thirty

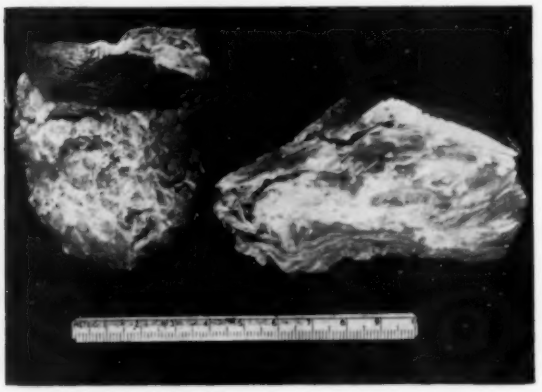

Fig. 3. Photograph of skin and subcutaneous tissue, showing distribution of calcium.

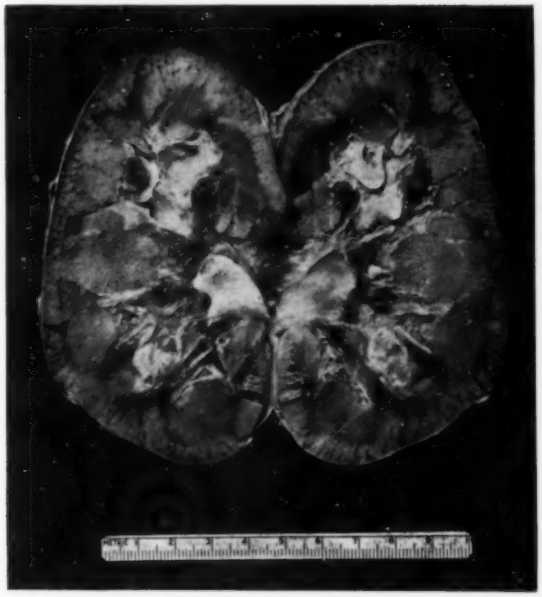

Fig. 4. Right kidney, showing several large and numerous minute concretions.

years of age, 155 cm. in length, weighing about 85 pounds. Over the posterior hip and sacral regions there were four healed and two unhealed circular punched-out ulcerations which measured from 5 to 8 cm. in diameter. There were a number of protruding freely movable subcutaneous masses, the largest of which occurred on the lateral aspect of the right arm and measured 17×6×1.5 cm. This mass was hard and had the contour of the underlying bone. A similar but smaller formation was present in the left arm. There was a large, ovoid, nodular bony hard mass felt just above the right iliac crest which bulged outward in the region of the right flank and measured 10×4.5×4 cm. There was another flattened oval mass in the subcutaneous tissue midway be-

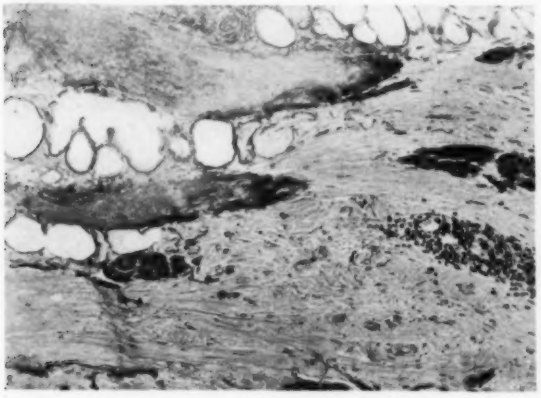

Fig. 5. Subcutaneous calcification and lymphocytic infiltration. ×170.

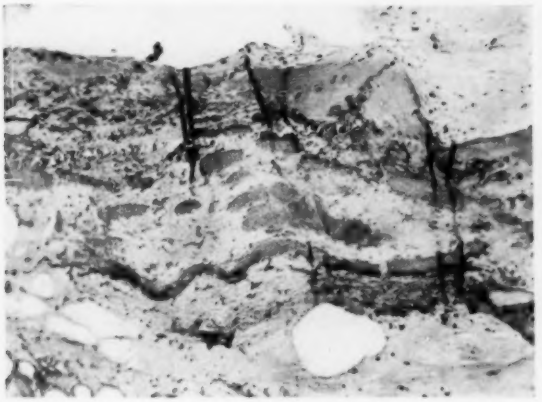

Fig. 6. Subcutaneous tissue showing bone formation within calcified area. ×170.

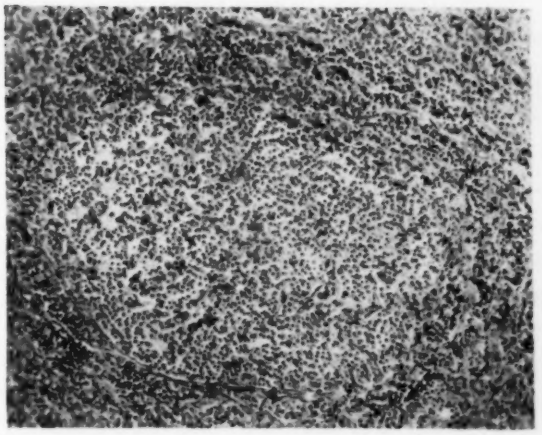

Fig. 7. Pituitary chromophobe adenoma. ×115.

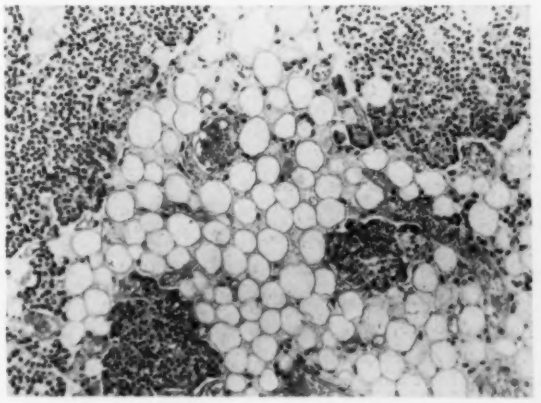

Fig. 8. Atrophy and fatty infiltration of parathyroid. ×175.

tween the umbilicus and the symphysis pubis just above the midline measuring 6 cm. transversely, 4 cm. vertically, and 2 cm. in thickness. Another protuberance of bony consistency was present in the right groin just below the inner half of the inguinal ligament and measured 7×5×2 cm. Other nodular formations were palpated in the following locations: the inner aspect of the left arm, the region of the bend of the left elbow, the outer aspect of the upper right forearm, the right lower quadrant of the anterior abdominal wall, the posterior aspect of the right flank, the upper outer aspect of the right thigh, the anterior aspect of the middle of the right thigh, and the upper outer aspect of the left thigh. The subcutaneous tissues showed increased fibrous tissue.

Gross Diagnosis: Acute dilatation of stomach; pulmonary atelectasis; decubitus ulcers; septic spleen; generalized subcutaneous areas of calcification; hyperplastic pelvic lymph nodes; enlarged parathyroid gland; bilateral nephrolithiasis; subarachnoid edema; scleroderma; emaciation.

Microscopical Diagnosis: Subcutaneous multiple calcifications with areas of bone formation; pituitary chromophobe adenoma; parathyroid atrophy and fatty infiltration; pulmonary atelectasis, fibrosis, chronic passive congestion and subacute pneumonitis; myocardial atrophy; atrophy of intestinal muscle; serous atrophy of epicardial fat; hyperplasia of reticulo-endothelial cells of liver, spleen, pelvic lymph nodes; subacute pyelonephritis; calcification within collecting tubules and calyces. Hemosiderin and hemofuscin pigment within epithelial cells of collecting tubules. Chronic ureteritis. Atrophic endometrium. Chronic endocervicitis.

A calculus removed from the pelvis of the right kidney weighed 2.37 gm., and upon analysis showed the presence of calcium phosphate, occult blood, oxalate, and ammonia. Cystine, xanthine, uric acid and urates were absent. Quantitative analysis showed calcium 7.0 per cent, magnesium 3.1 per cent, phosphorus 8.0 per cent and cholesterol 0.45 per cent.

COMMENT

In calcinosis universalis, the calcifications are multiple and widespread and occur in the skin, subcutaneous tissues, muscles and tendons. In calcinosis circumscripta, the deposits are mainly located in the extremities, particularly about the joints. In the metastatic calcification of Virchow, unlike calcinosis, calcium is lost from the bones, saturates the blood, and then is deposited in the tissues, which show no degeneration.

Etiology. Ham[5] divides pathologic calcifications into two groups. In one group there are degenerative or physical changes in recipient tissues, as in breaking down of fats into soaps, with later permanent deposits of calcium. In the other group there is a change in the blood so that it may become unable to retain all its calcium in solution, as in metastatic calcifications associated with certain parathyroid tumors that produce hyperparathyroidism. In his opinion calcifications do not necessarily appear to result from hypercalcemia. Ham suggests that calcifications of the variety that depend on the inability of the serum to retain all its calcium in solution depend for their causation to a greater extent on the level of diffusible calcium than on the level of the total serum calcium. In the reported cases of calcinosis the blood calcium value was usually normal. According to Rothstein and Welt[10] no changes in the parathyroids have been observed in calcinosis. Shelling[11] mentions the finding of amyloid infiltration of the parathyroids in a patient with generalized calcinosis and amyloidosis without tetany in whom the concentration of serum calcium and inorganic phosphorus fluctuated between normal and tetanic levels. Most authors are of the opinion that calcium salts may be deposited in normal tissue which show no antecedent degeneration or inflammatory change. Epstein et al.[4] suggest that the frequent association of scleroderma and calcinosis may indicate a common etiology and that the sclerodermic process may be preparatory to calcification. Among the suggested etiologic factors are the endocrines, infection, trauma, disturbances in the local vascular supply, a disturbance in the local acid-base equilibrium, and the presence of lipolytic ferments in the sub-

cutaneous tissue. Scleroderma was found in 11 of the 39 cases of calcinosis reviewed by Rothstein and Welt, while infection was a possible etiological factor in 9 cases.

Pathology. Jadassohn,[8] reporting on the histology of calcinosis universalis, states that the calcareous material lies in the true skin between the collagen fibrils, affecting the elastic fibers and is distributed diffusely. Bauer et al.[1] described the earliest signs of calcification as consisting of finely divided particles around apparently healthy normal fat cells in subcutaneous tissue, occurring without evidence of necrosis or inflammation. The process continues until whole fat lobules are replaced by deeply staining homogeneous masses of calcified material. The biochemical findings of the blood in this group are variable, inconclusive, and show normal readings in many cases. Brooks[2] found that the fat cells adjacent to the calcified areas are filled by a pink staining homogeneous material which he thought was protein exudate, which resembles that seen in fat necrosis and suggests that the calcifications might be secondary to degenerative changes in the fat.

Of the 32 cases of calcinosis universalis in children reviewed by Rothstein and Welt, 3 came to necropsy. Dietschy's patient, a girl of thirteen, at necropsy showed extreme cachexia, dermatomyositis interstitial myositis, atrophy of skin, calcareous deposits along the tendons, perivascular infiltration of muscles of heart, bladder, and uterus. Tisdall and Erb's patient, a boy of nine weeks, showed at autopsy a patella that was largely cartilaginous with loose connective tissue scattered throughout the cartilage; degenerative changes in connective tissue with calcific deposits in degenerated areas, but no inflammation. In one of Rothstein and Welt's cases, a girl of eleven years, autopsy revealed terminal pneumonia, dermatomyositis, degenerative changes in the skin, muscles and fibrous connective tissue; calcific deposits in degenerated fibrous connective tissue, tuberculosis of lung and bronchial lymph nodes. A fourth case, that of Bruusgaard, a boy of fourteen, died of pulmonary tuberculosis, but did not come to autopsy.

Treatment. Brooks recommends a restriction in the intake of calcium and milk and the administration of sodium dihydrogen phosphate. Craig and Lyall[3] reported a case of calcinosis universalis in a girl of five years which disappeared after six weeks of oral medication with disodium phosphate. Hamlin[6] reported a case of extensive calcareous deposits in the hand and and arm of a twenty-three year old male which were observed over a period of five years and improved remarkably without treatment. In Hein's[7] case of calcinosis, a girl of six and one-half years was successfully treated over a period of four years by heliotherapy. Weber[12] observed improvement in a case of calcinosis universalis in a child of seven years who received medication with syrup of iodide of iron and potassium iodide, the calcified nodules having markedly decreased as seen by roentgen examination. During the period of a year of treatment, the blood calcium was considerably raised. Kennedy[9] reported a case of calcinosis with scleroderma in a girl of six years in whom the calcareous deposits disappeared during treatment by a ketogenic diet. Bauer et al.[1] obtained improvement in their case by the use of ammonium chloride.

SUMMARY

In our case the factors of possible etiologic significance were the ingestion of a large quantity of vinegar, excessive reduction in weight, infection (abscess of breast, furunculosis of skin), scleroderma, pituitary chromophobe adenoma, and atrophy with fatty infiltration of an enlarged parathyroid gland. The nephrolithiasis would appear to be a manifestation of the general calcinosis and the pyelonephritis and ureteritis would seem to be secondary to the nephrolithiasis. Our patient showed progressive wasting, muscular atonia, irritability, generalized tenderness and pain, and weakness, all of which symptoms may be due to a faulty calcium metabolism, de-

spite the normal blood calcium findings. Death from emaciation occurred two years and three months after the onset of symptons.

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VOL. 39, NO. 5

LEUKOPENIA AND LEUKOCYTOSIS IN LYMPHOBLASTOMA

THEIR REACTION TO ROENTGEN THERAPY*

By FRED H. DECKER, M.D.
Methodist Hospital, Peoria, Illinois,
EUGENE T. LEDDY, M.D., *and* ARTHUR U. DESJARDINS, M.D.
Section on Therapeutic Radiology, The Mayo Clinic
ROCHESTER, MINNESOTA

OVER one hundred years ago, in 1832, Hodgkin[16] described a group of diseases characterized by hyperplasia of the lymphoid elements of the body and an invariably fatal termination. This group has been gradually divided and subdivided into the many so-called entities known today.

Since their advent, roentgen rays have played a large part in the treatment of lymphoblastoma, and they are now generally accepted as the best means of bringing about remissions, although Coley's[6] toxins and autogenous gland filtrates[13] are lauded in some quarters. The results of Desjardins and Ford,[8] and of Minot and Isaacs,[25] have sounded the general sentiment of what might be expected from this form of treatment of lymphoblastomas. They found that only a little time is added to the length of life of the patient, but that irradiation does exert a beneficial influence by bringing about relatively long periods of remission and curtailing to a minimum the period of actual disease.

Even though the benefits may be great, the character of this method of treatment suggests caution in its use, since there are definite contraindications, as well as conditions demanding painstaking care in bringing about the desired remission. The acute, malignant lymphomas, which cause acute illness, high fever, and marked toxemia, call for conservation in treatment. Also, the patient who exhibits large, fluctuating, infected, swollen lymph nodes must be treated conservatively. Leukopenia has been mentioned as a direct contraindication to roentgen therapy, but since experience at The Mayo Clinic has not led us to agree with this view, an analysis of a series of cases of lymphoblastoma treated in the Section on Therapeutic Radiology is presented.

NATURE AND CLASSIFICATION OF LYMPHOBLASTOMAS

Medical literature contains much speculation concerning the nature of the lymphoblastomas, and the terminology applied to these growths differs so markedly in the various publications that a consideration is incomplete unless each entity is carefully defined. The term lymphoblastoma includes Hodgkin's disease, lymphosarcoma and possibly lympho-epithelioma. In this paper, the object is to consider Hodgkin's disease and lymphosarcoma exclusively.

While Hodgkin first attracted attention to the lymphoid diseases, Wilks,[37] in 1856 and 1865, followed by Sternberg,[34] in 1898, Longcope,[20] in 1901, and Reed[31] in 1902, defined Hodgkin's disease as it is understood today. Their conception included gradual progressive enlargement of the lymph nodes, beginning usually in the cervical region and spreading throughout the lymphoid tissues of the body, forming nodular growths in the internal organs, and resulting in anemia and usually fatal cachexia. The present conception of lymphosarcoma as a true sarcoma of the lymphoid structures dates back to Kundrat,[17] in 1893. Histologically he described them as follows.

Lymphosarcoma is characterized by reticular basic tissue with embedded lymphoid cells; it must be stressed here that it is never the same

* Abridgment of thesis submitted by Dr. Decker to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Roentgenology, 1932.

as the normal reticulated lymphoid tissue because the irregular stroma undergoes more or less fibrosis and contains an abundance of cells of increased size and of different type. It does not remain confined to the lymph node to form a single tumor of the follicle and node but breaks through the boundaries of the follicle and the capsule of the node to infiltrate the surrounding tissues. The nodes become matted together.

In Hodgkin's disease there is hyperplasia of all types of cells present in a normal lymph node, including the large and small lymphoid cells, fibrocytes, reticular cells, granular leukocytes (mostly eosinophiles), a peculiar type of giant cell described by Reed,[31] and complete loss of the structural characteristics of the node. Similarity in the appearance of lymphoblastomas and inflammatory granulomas is marked, and in the series reviewed as the basis of this paper, the pathologic diagnosis of inflammatory tissue was occasionally made. However, the typical enlargement of the nodes, their characteristic consistence and distribution, their exceptional response to roentgen therapy, their subsequent recurrence, and their diminishing susceptibility to radium or roentgen rays, suggested strongly that the cases were examples of lymphoblastoma. In this regard, Desjardins[7] suggested that the response of a tumor to roentgen therapy may give a clue as to the nature of the tissue being dealt with.

The relationship of Hodgkin's disease and lymphosarcoma to each other is apparently close. Mueller,[28] Sternberg,[34] Gibbons,[11] Minot and Isaacs,[25] Coley,[6] Warthin,[36] Broders,[4] and others, have suggested this similarity. Many authors go so far as to suggest that these two diseases are phases of leukemia.

BLOOD PICTURE

Agreement is almost unanimous that in most cases the diagnosis of Hodgkin's disease from the blood picture is impossible. Secondary anemia, moderate at first, progressing with the course of the disease, seems to be the most constant feature. At various times, eosinophilia, lymphopenia, or an increase in the number of monocytes or blood platelets have been cited by different authors as pathognomonic of this condition.

Desjardins and Ford found leukocytosis common in a series of 237 cases, more so in Hodgkin's disease than in lymphosarcoma. In the former, eosinophilia of 88 per cent and a total leukocyte count of 83,000 cells in each cubic millimeter of blood occurred in individual instances; also, however, leukopenia (3,000) was noted. In 12 cases of lymphosarcoma there was definite leukocytosis. In one case, in which diagnosis was proved by biopsy, the leukocytes numbered 247,000, of which 93 per cent were lymphocytes. In 4 cases there was leukopenia.

Leukopenia is an occasional complication of lymphoblastoma, as has been noted by Gütig,[12] Meyer,[23] Mellon,[22] and Miller.[24] A total leukocyte count of less than 5,500 is occasionally noted in examination of normal, healthy persons, and it is obvious that such a person has an equal opportunity of developing either Hodgkin's disease or lymphosarcoma. The assumption has been general that leukopenia connotes the terminal stages of this condition, although McAlpin[21] definitely contradicted this hypothesis, and Fabian,[10] Bunting,[5] and others suggested the opposite, that leukocytosis is characteristic of the terminal stage. The suggestion also has been made frequently that roentgen therapy might be a factor in producing leukopenia, although in the practical therapeutic use of roentgen rays the danger of depletion of leukocytes is assumed and guarded against.

Experimental work indicating the effect of roentgen rays on the blood was begun by Heineke[15] in 1904. After irradiating animals he found the lymphoid tissue primarily affected, and this was accompanied by diminution of circulating lymphocytes. The leukocyte count was lowered, but the percentage of neutrophiles was increased. The doses used on experimental animals would correspond to large doses of short wave length used on man. Aubertin and Beau-

jard[2] were the first to note the occurrence of a slight, transient increase in the total number of leukocytes, mostly of polymorphonuclear neutrophiles, immediately after irradiation. This was followed by lymphopenia, and in some cases, if the amount of irradiation had been large enough, by leukopenia. It is apparent that the greater the amount of radiation absorbed, the greater the leukopenia. Heim[14] indicated that the leukocyte count may remain low for from three to five weeks before it returns to the normal level. Benjamin[3] and his associates suggested that regeneration takes place more quickly when the circulating blood rather than the blood-forming tissues is exposed to the roentgen rays. Mottram[27] and Murphy[29] expressed the thought that a small dose might stimulate the lymphocytes and thus cause lymphocytosis, while there might be an absolute decrease but not a percentage drop in polymorphonuclear neutrophiles. According to Aubertin and Beaujard, shortly after irradiation the blood may contain leukocytes undergoing premature death, and later, when regeneration takes place, youthful cells are seen. Erythrocytes and blood platelets undergo little change except when the irradiation is intense and long continued. Minot and Spurling[26] pointed out the changes in the blood in a series of cases in which rays of short wave length were used. They found a slight, early rise in the leukocyte count, due to the increase of polymorphonuclear neutrophiles, followed by a drop involving particularly the lymphocytes, so that lymphopenia and leukopenia might occur. The lowest point was reached in six days, and remained for nine days, complete regeneration usually taking place in a month. Stronger irradiation produced more rapid, marked, and persistent changes; the size, intensity and character of the dose, as well as the surface area exposed, were the determining factors. Degenerated leukocytes were noted one to three days after irradiation, and immature forms were reported when regeneration took place. The investigators concluded that patients with 5,000 or more leukocytes in each cubic millimeter of blood might be safely treated, that even in the presence of leukopenia, treatment could be carried out without disaster, and that desirable therapeutic irradiation might produce only slight alterations of the blood. Several years later, Stetson[35] corroborated the findings of Minot and Spurling. In his series, 8 per cent of patients had leukocyte counts of between 5,000 and 6,000, whereas only 1 per cent had counts of less than 5,000. After the first course of irradiation, 26 per cent of patients had less than 6,000 leukocytes; the level before treatment was regained at the end of approximately eight weeks. Following the second course, the results were about the same, whereas, among 10 patients who had three courses, leukopenia did not develop. Peculiarly, while in the 28 cases in which leukopenia developed a slightly greater dosage had been given and a greater area had been irradiated, the mortality was not as great, or death as prompt, as in the others. The lower leukocyte counts dropped 36 per cent after irradiation, compared with 13 per cent among the higher counts. Piney[30] agreed essentially with Stetson and with Minot and Spurling, adding that persistence of leukopenia was due to injury of the hematopoietic system from the roentgen rays.

Previously, Desjardins and Marquis,[9] in 1924, had reported that the lymphocytes were the most sensitive to irradiation, and noted an early, rapid reduction in the proportion of them. The polymorphonuclear leukocytes were primarily increased, and this increase was followed by rapid diminution. In their series, regeneration of both types of cells occurred; this regeneration was dependent on the dose of roentgen rays applied. In this regard, it is important to recall that regeneration takes place relatively early with the doses used in the treatment of lymphoblastoma, and that therefore there should be no great lowering of the leukocyte count unless the cells were diseased, or were obviously too numerous. Levin,[19] in a recent paper, agreed that lym-

phocytes are more readily influenced by radium or roentgen rays than are other blood cells, but he also suggested that normal lymphoid tissue is much less radiosensitive than the various types of lymphoid hyperplasia, and further, that simple inflammatory hyperplasia is less radiosensitive than neoplastic hyperplasia. From this it could easily follow that diseased lymphocytes would be present in the blood stream in cases of lymphoblastoma. Desjardins and Marquis expressed the belief that their results were due to the direct action of the rays on the cells in the lymph nodes and blood stream rather than on the blood-forming tissues. Akaiwa and Takeshima[1] found that the final result of irradiation of a lymph node was fibrosis of the lymphoid elements. However, their doses were extremely large in comparison with those of other authors and it is obvious that if smaller doses are used, with a fairly long interval between them, lymphoid tissue cannot be so affected that a latent effect, causing ultimate lowering of the leukocyte count, can result. Apparently in the treatment of the conditions under consideration, only the early reduction in the number of leukocytes is feared, and since marked regeneration of the leukocytes is noted after irradiation, latent effects are probably of no significance.

It is almost axiomatic among roentgenologists that leukopenia is a contraindication to radiotherapy. The conclusions of Seitz and Wintz,[32] Piney, and others have resulted from experience with the use of short wave length irradiation in the treatment of carcinoma of the uterine cervix and like conditions. These conclusions unconsciously have been applied to the smaller doses in which radiation of longer wave length was used, in spite of the knowledge that injury to blood was dependent on the volume dose applied.

TECHNIQUE

Early in Hodgkin's disease and lymphosarcoma, a mild dose of moderate voltage* roentgen therapy accomplishes as much as those given with high voltage.† According to Leddy,[18] high voltage treatment should be restricted to the later and refractory stages of the disease. Leddy stated this principle in connection with the treatment of chronic myelogenous leukemia, but indicated that the same theory would apply to the treatment of all lymphoblastomas.

The first course usually consists of exposure to roentgen rays of all node-bearing areas which are prone to be affected by the disease, and takes five to twelve days to complete. Figures 1 and 2 illustrate what is understood as a complete treatment, indicating the areas treated and the technical factors. Figure 1 is the outline of treatment for patients with massive mediastinal and retroperitoneal involvement, and Figure 2 for those who have moderate involvement of superficial nodes. Variations from these outlines are determined by the physical condition. Three weeks after completion of the first course, the patient returns; usually the physical condition is markedly improved, and the enlarged nodes are reduced in size, but a complete second course is generally given. Then, after a similar interval, the patient is seen for the third time, and if evidence of the disease is still present, a third, less extensive course is applied to the involved areas. After the patient has received two or three such courses, additional treatment is governed largely by recurring lymphadenopathy and its distribution. In the later stages, high voltage (200,000) may occasionally be resorted to.

SURVEY OF CASES TREATED AT THE MAYO CLINIC

The records of 450 cases of lymphoblastoma observed at The Mayo Clinic were studied with particular reference to the leukocyte count on admission, before any roentgen therapy was administered. The diagnosis was made by biopsy in almost three-fourths of the cases; in others, if the masses were inaccessible for biopsy, the response to roentgen therapy and the clinical

* Moderate voltage consists of 135,000 volts, 5 ma., 40 cm. distance, either 4 or 6 mm. of aluminum and eighteen to thirty minutes of exposure.

† High voltage consists of 200,000 volts, 5 ma., 50 cm. distance, filtration of 0.75 mm. of copper and 1 mm. of aluminum, and sixty to seventy minutes of exposure.

course were typical of lymphoblastoma. In a few cases, the history, physical condition, and clinical course were deemed sufficient, especially in view of the improvement after roentgen therapy. In a few others, the leukopenia; (2) 20 cases in which the leukocyte count was normal, and (3) 20 cases in which there was leukocytosis. Groups 2 and 3 were selected entirely on the basis of the leukocyte count before treatment was be-

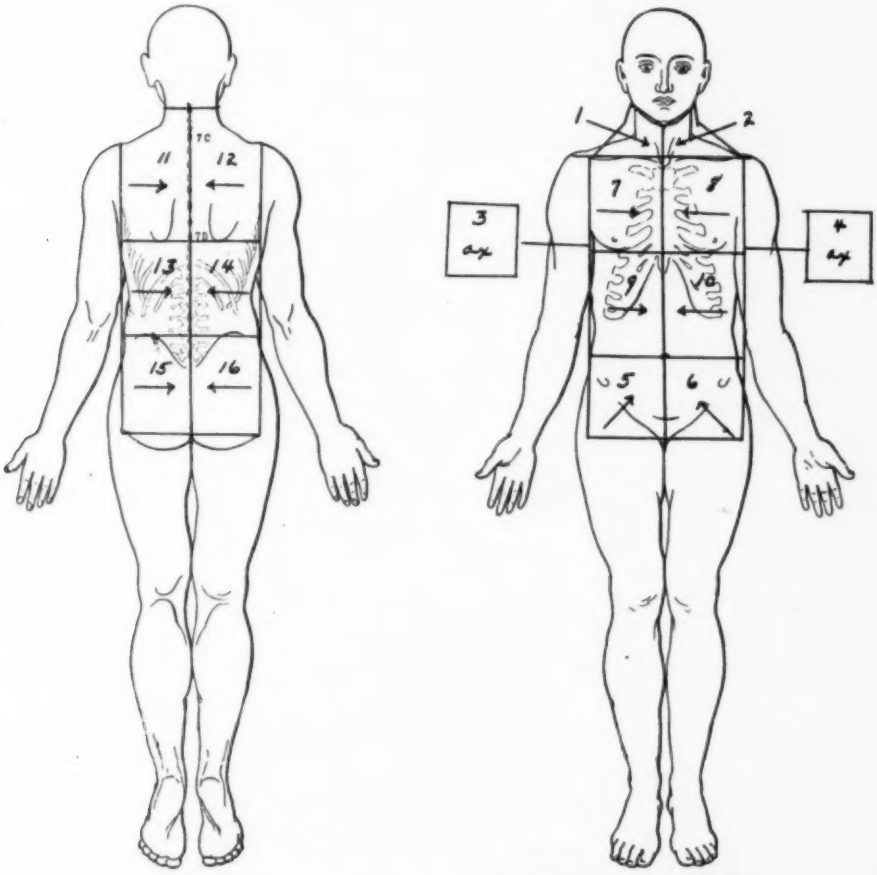

FIG. 1. Schema of treatment and technical data for patients with mediastinal and retroperitoneal involvement. Areas 1 to 6 inclusive: kv. 135; filter 4 mm. Al; distance 40 cm.; ma. 5; time 18 min. Areas 7 to 16 inclusive: kv. 135; filter 6 mm. Al; distance 40 cm.; ma. 5; time 28 min.

report of biopsy was other than lymphoblastoma, but here again the response was so typical, and clinical evidence so great, that little hesitation was felt in considering them as cases of lymphoblastoma.

In the following survey leukocyte counts of 5,500 or less will be considered evidence of leukopenia; from 5,500 to 10,000 inclusive, normal, and counts of more than 10,000, evidence of leukocytosis. Each of these states will be represented by a group of cases, selected on the basis of the leukocyte count: (1) 25 cases in which there was gun. However, Group 1 was subdivided. In 6 of these cases, roentgen therapy had been given elsewhere shortly before the patients came to The Clinic, and it was impossible to know what the leukocyte count had been before treatment began.

In the remaining 19 cases roentgen therapy was first given at The Clinic, and the leukocyte count before treatment began was known. It is also to be noted that the records of many of these 19 patients with leukopenia were not complete, since the patients came from a distance, and in some

instances further treatment was arranged for at home. In some instances, records of blood counts were lost or counts were not made, or other necessary observations were not taken.

The subgroup of 6 patients with initial leukopenia presented themselves with leukocyte counts varying between 2,800 and 5,800, (average 4,266) and since it is conceivable that the leukopenia may have been caused by the treatments given before they came to The Clinic, the cases should be considered separately. The technical details of the treatment given before admission could not be ascertained; in some instances it was adequate; in the majority, it apparently was not. Several patients had been exposed three or four times for three to four minutes. The duration of the disease varied from three months to two years, averaging about a year. Table I indicates the differential count at the first visit and Table II indicates the date of visits, the leukocyte count, and the treatment given at each visit. From these few data it appears that even though roentgen treatment was given once in each case and twice in 5 of the 6 cases, the leukocyte count at the end of the second or third visit was either equal to or higher than the original count.

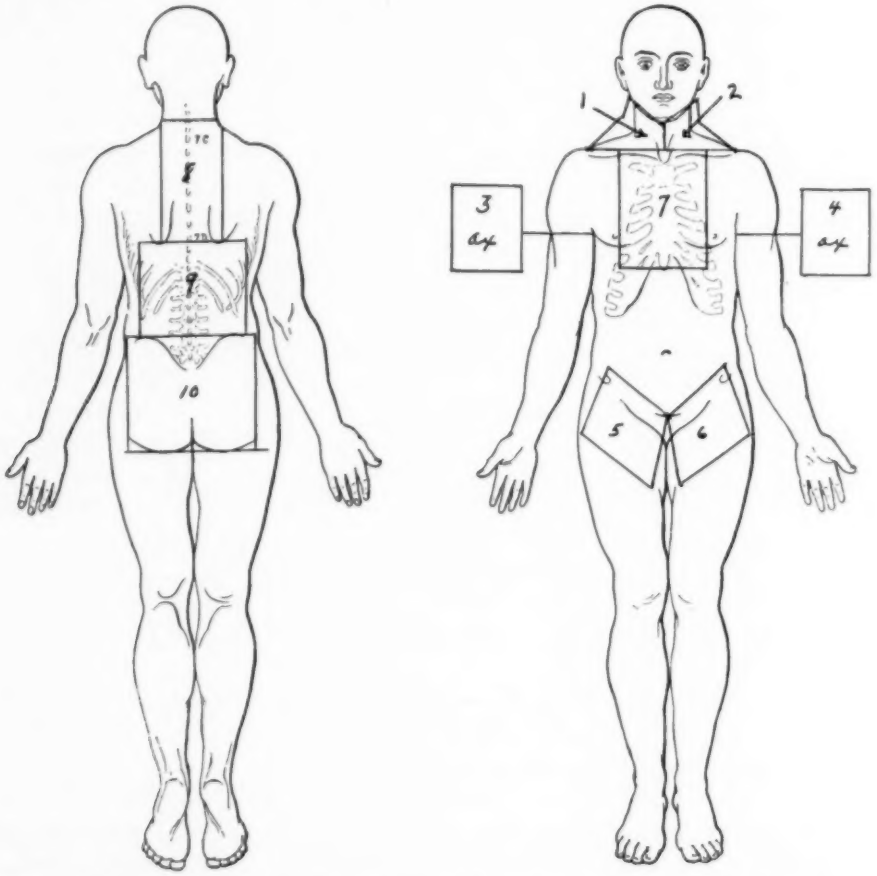

FIG. 2. Schema of treatment for patients with moderate superficial involvement of the nodes and no mediastinal or retroperitoneal lymphadenopathy. Areas 1 to 6 inclusive: kv. 135; filter 4 mm. Al; distance 40 cm.; ma. 5; time 18 min. Areas 7 to 10 inclusive: kv. 135; filter 6 mm. Al; distance 40 cm., ma. 5; time 28 min.

Analysis of the remaining 19 cases (Table III), in which there was initial leukopenia, throws little light on the various fac-

TABLE I

TOTAL AND DIFFERENTIAL* LEUKOCYTE COUNTS OF PATIENTS ADMITTED TO THE CLINIC WITH INITIAL LEUKOPENIA, WHO HAD HAD PREVIOUS ROENTGEN TREATMENT

Case	Total leukocytes, for each cu. mm. of blood	Lymphocytes, per cent	Polymorphonuclear neutrophiles, per cent	Transitionals, per cent	Eosinophiles, per cent	Basophiles, per cent
1	4100					
2	3800	20.5	70.5	3.5	2.0	1.0
3	2800	47.0	41.0	8.0	0.0	0.0
4	4000					
5	5100	19.5	74.5	5.0	1.0	0.0
6	5800	15.5	57.5	2.5	21.0	1.0
Average	4266	25.6	60.9	4.7	6.0	0.5

* Large mononuclears averaged 2.3 per cent.

tors that might be considered to have caused, or at least to have contributed to, the presence of leukopenia.

The group of 20 cases in which the leukocyte count was initially normal and the group of 20 cases in which the initial state was one of leukocytosis are compared with the 19 cases in which there was initial leukopenia. This comparison was made in order to show that leukopenia is not accom-

TABLE II

TOTAL LEUKOCYTE COUNTS AND DATES OF TREATMENTS OF SIX PATIENTS WHO HAD HAD PREVIOUS ROENTGEN TREATMENT

Case	First Visit	Second Visit	Third Visit	Fourth Visit	Fifth Visit
1	2–10–30 4100 Rx*	3–13–30 Rx—No C.†	4–14–30 8100 Rx		
2	4–28–29 3800 Rx	5–13–29 3300 Rx	7–24–29 5900 Rx	12–2–29 4500 Rx	
3	6–11–30 2800 Rx	9–13–30 3900– 4700Rx			
4	9– 8–30 4000 Rx	9–25–30 5000– 5700 Rx			
5	10–22–29 5100Rx	11–26–29 2600 P.Rx‡			
6	6–21–29 5800 Rx	7–15–29 3300 P.Rx	9– 9–29 5400 P.Rx	12–11–29 5300 Rx	2–18–30 4200 Rx
Average count	4266	3780	6466	5900	

* Rx = treatment.
† No C. = no count.
‡ P. Rx = partial treatment.

TABLE III

TOTAL AND DIFFERENTIAL LEUKOCYTE COUNTS OF PATIENTS WITH LEUKOPENIA BEFORE TREATMENT (5,500 AND LESS)

Case	Total leukocytes for each cu. mm. of blood	Lymphocytes, per cent	Polymorphonuclear neutrophiles, per cent	Transitionals,* per cent	Eosinophiles, per cent	Basophiles, per cent	Large mononuclears,* per cent
7	4300	26.0	70.0	0.0	3.0	0.0	1.0
8	4900	21.5	66.5	5.0	5.0	1.0	1.0
9	4800	17.5	72.0	4.5	3.5	0.0	2.5
10	5000	21.5	71.5	2.5	0.5	0.0	4.0
11	3900	35.0	47.0	9.0	1.0	2.5	5.5
12	5300	27.5	66.5	3.5	0.5	0.5	1.5
13	4100						
14	4700	35.0	54.0	0.5	5.5	0.0	0.5
15	4900	28.0	65.0	0.0	3.0	0.5	3.5
16	4400	36.5	51.5	6.0	1.5	1.5	3.0
17	4000	20.0	61.0	0.0	16.0	0.0	3.0
18	4400	28.0	56.5	6.0	7.5	0.0	2.5
19	5400	20.5	63.5	0.0	8.5	0.0	7.5
20	5900	21.5	72.0	4.0	1.0	0.5	1.0
21	5100						
22	4100						
23	4800	20.0	76.5	2.5	0.0	0.0	1.0
24	3900	35.0	62.0	2.0	0.0	0.0	1.0
25	4400						
Average	4626	26.2	63.7	3.1	3.8	0.4	2.6

* These two groups, the transitionals and large mononuclears, are more properly placed together under the heading monocytes.

panied by other distinctive factors which would place these patients with leukopenia in a class apart from those with normal leukocyte counts or with leukocytosis.

Tables III to V inclusive, indicate the total leukocyte and differential counts on admission in the various groups. These show little variation except for mild lymphopenia in the group with leukocytosis and an increase of the percentage of lymphocytes in the group with leukopenia.

Tables VI to X show the comparison factors of age, sex, biopsy, presence of fever, size, situation of nodes, and duration of disease before treatment. Admittedly the manner of arriving at some of the statistics is unsatisfactory. It is evident, for instance, that the determination of the time of onset of a lymphogranulomatous disease, as given by the patient, is extremely unreliable. Several of the patients came to The Clinic complaining of weakness, malaise, and pain, but were totally unaware of the presence of lymphadenopathy. Others had had enlarged nodes since childhood, and it was impossible for them to know exactly when the change took place. Even though one accepted the beginning of malaise and weakness as the beginning of these diseases, several of the patients had been ill from other causes, and it is improbable that the time of transition could have been noted. Furthermore, it is well known that the onset is often insidious, the patient being totally unaware of the presence of the disease until the nodes have enlarged so as to cause sufficient pressure on adjacent structures to produce symptoms, and abdominal glandular enlargement may be huge before it is discovered. The presence of fever is also a variable factor. This may be of the Pel-Ebstein type, periodic pyrexia, which may not be present at the time of admission and may have been so slight that it was not

noted by the patient previous to his seeking medical aid. An attempt has been made, from the diagram of the lymphadenopathy treated, and which appears on the history sheets, to arrive at some conclusion concerning the size of the masses with reference to the presenting leukocyte count. Some had not been measured, but it is obvious that in most instances the measurement of a mass through skin, superficial tissues and deep tissues is unsatisfactory and only approximate, particularly if abdominal and paravertebral nodes are involved. For that reason, an attempt has been made to arrive at an estimate of the size by classifying the nodes as small, moderate and massive. Those rated as "small" appear to have been about 2 cm. or less in diameter, those designated as "moderate" between 2 and 5 cm. in diameter, and those with diameters of more than 5 cm. are grouped as "massive." It is admitted that this is a very inaccurate method, but it will serve to give a rough idea as to whether size of nodes has any relationship to a low leukocyte count. Many symptoms, other than fever and pruritus, are frequently dependent on the size and situation of the enlarged nodes; hence, no attempt has been made to determine the frequency of occurrence of the many symptoms which may be present.

Examination of Tables VI to X elicits little by which patients with a low leukocyte count could be distinguished from the others by means only of the factors presented. Leukopenia occurred slightly more often among females (Table VI) and also in a slightly younger age group. The differences are not sufficient to indicate anything more than normal variation. The frequency of lymphosarcoma in the group with low initial leukocyte counts, and of Hodgkin's

TABLE IV

TOTAL AND DIFFERENTIAL LEUKOCYTE COUNTS OF PATIENTS WITH NORMAL COUNTS BEFORE TREATMENT (5,500 TO 10,000)

Case	Total leukocytes for each cu. mm. of blood	Lymphocytes, per cent	Polymorphonuclear neutrophiles, per cent	Transitionals,* per cent	Eosinophiles, per cent	Basophiles, per cent	Large mononuclears,* per cent
26	7800	22.0	71.0	4.0	2.5	0.5	0.0
27	8700	26.5	60.0	2.0	5.5	1.0	5.0
28	6700	22.5	72.5	1.0	2.5	0.5	1.0
29	8600	27.0	63.0	0.0	4.0	1.0	5.0
30	8400	14.5	73.0	2.5	7.0	0.5	2.5
31	6100	29.5	64.5	4.5	0.0	0.5	1.0
32	9200	3.5	98.0	6.0	0.5	0.0	2.0
33	8800	23.0	70.0	4.0	1.0	1.0	1.0
34	6200	38.0	53.5	3.5	4.0	0.5	0.5
35	7000	20.0	77.0	2.0	0.5	0.0	0.5
36	6600	23.0	66.5	2.0	7.5	0.0	1.0
37	7700	27.5	62.5	4.0	1.5	1.0	3.5
38	7400	25.5	67.0	2.0	2.5	1.5	1.5
39	8200	24.5	66.5	3.0	3.5	1.0	1.5
40	7100	27.0	66.0	2.0	3.5	0.0	1.5
41	8100	25.0	60.5	8.5	2.0	1.0	3.0
42	6100	17.0	76.0	3.5	0.5	0.5	2.5
43	7100	18.0	75.0	1.0	0.0	0.0	6.0
44	7500	12.0	83.5	0.5	0.5	1.5	2.0
45	8400	27.5	62.0	3.5	3.5	0.5	3.0
Average	7585	21.67	69.4	2.97	2.6	0.6	2.2

* These two groups, the transitionals and large mononuclears, are more properly placed together under the heading monocytes.

TABLE V

TOTAL AND DIFFERENTIAL LEUKOCYTE COUNTS OF PATIENTS WITH LEUKOCYTOSIS BEFORE TREATMENT (MORE THAN 10,000)

Case	Total leukocytes for each cu. mm. of blood	Lymphocytes, per cent	Polymorphonuclear neutrophiles, per cent	Transitionals,* per cent	Eosinophiles, per cent	Basophiles, per cent	Large mononuclears,* per cent
46	19300	4.0	87.5	4.5	1.0	0.0	3.0
47	15200	18.5	78.0	3.0	0.0	0.5	0.0
48	15400	14.0	77.5	1.5	2.5	0.0	4.5
49	11000	20.5	76.5	1.5	1.0	0.0	0.5
50	12000	21.5	73.5	1.0	3.0	0.5	0.5
51	29700	5.0	90.5	1.0	2.0	0.5	1.0
52	10700	17.5	72.0	2.0	1.5	0.5	6.5
53	23100	11.5	42.5	2.0	42.0	0.0	2.0
54	18800	6.0	88.5	2.0	0.5	0.0	3.0
55	15100	15.0	75.0	2.5	5.0	0.0	2.5
56	13200	18.5	78.0	1.5	1.0	0.0	1.0
57	14400	18.0	76.5	2.5	2.5	0.0	0.5
58	15000	14.5	81.0	0.0	2.5	2.0	0.0
59	12600	17.5	75.0	4.0	0.5	1.5	1.5
60	16900	5.5	91.0	1.0	0.5	0.0	2.0
61	14300	13.0	78.5	5.0	3.0	0.0	0.5
62	24000	16.5	82.0	0.5	1.0	0.0	0.0
63	13900	23.5	71.5	2.5	1.0	0.0	1.5
64	16500	23.0	71.0	2.5	0.5	0.5	2.5
65	10300	14.0	79.0	3.5	3.0	0.0	0.5
Average	16070	14.9	77.3	2.2	3.7	0.3	1.7

* These two groups, the transitionals and large mononuclears, are more properly placed together under the heading monocytes.

disease in the group with initial leukocytosis (Table VII) may have some significance. The amount of involvement (Table VIII) is practically the same, except that splenic enlargement occurred three times as often in the group with initial leukopenia, and enlarged epitrochlear glands were noted twice in that group, compared to none in the other two groups. This may be of value if epitrochlear involvement and splenic enlargement are considered as indicative of a more generalized stage of the disease. The

TABLE VI

INCIDENCE BY SEX AND AGE

	Group with initial leukopenia	Group with initially normal counts	Group with initial leukocytosis
Patients	19	20	20
Males	14	17	16
Females	5	3	4
Average age, years	34	39	35.5
Youngest	6	24	10
Oldest	60	63	53

TABLE VII

DIAGNOSIS BY BIOPSY

	Group with initial leukopenia	Group with initially normal counts	Group with initial leukocytosis
Lymphosarcoma	7	6	
Hodgkin's disease	7	3	15
Lymphoblastoma		1	
Inflammatory change		3	1
Malignancy graded 4		1	
Suggestion of leukemia		1	
No biopsy	5	5	4

size (Table IX) of the enlarged nodes was about the same. The only apparent difference exists in the duration (Table X) of the disease before treatment. This, however, is more apparent than real, for in a small series, the statistics on one patient may cause the average to be misleading. The patient represented by Case 13 gave a history of disease of eight years' duration before admission to The Clinic, which is almost twice the duration before treatment of any other case of the entire series. Cases occur occasionally which happen to be unusually chronic. This chronicity is due either to comparatively high resistance of the patient or to low activity of the disease. Such cases occur, alike, among treated and untreated patients. If this one case is disregarded, the average duration of the disease in the group with initial leukopenia would be thirteen months before the first treatment which compares favorably with the eleven and thirteen months of the other two groups. It seems, then, that these many factors vary only slightly, certainly not sufficiently to justify the conclusion that the patients with initial leukopenia are in the terminal stages of the disease. There is then no valid reason for withholding from them the beneficial effects of roentgen therapy.

Table VIII

FREQUENCY OF INVOLVEMENT OF VARIOUS GROUPS OF NODES

Group of nodes	Group with initial leukopenia, per cent	Group with initially normal counts, per cent	Group with initial leukocytosis, per cent
Cervical	73	80	85
Axillary	52	65	35
Inguinal	52	75	70
Mediastinal	10	30	50
Abdominal	15	25	10
Spleen	15	5	5
Epitrochlear	10		

As far as the records would permit, analysis of the effect of irradiation on the leukocytes and on the subsequent length of life was made. It will be recalled that treatment was applied at intervals of three or four weeks, and that because the patients frequently lived many miles away, some of the courses of irradiation were given at home. Consequently, many of the patients could not be traced from month to month, which would constitute the ideal method of follow-up. In several instances, the patients (in the group with initial leukopenia) were at The Mayo Clinic for only one course of treatment, and these will be omitted in a consideration of the effect of irradiation on the total leukocyte count in

Table IX

APPROXIMATE SIZE OF NODAL MASSES AND PRESENCE OF FEVER AS DETERMINED AT FIRST EXAMINATION

	Group with initial leukopenia	Group with initially normal counts	Group with initial leukocytosis
Large masses	11	9	9
Masses of moderate size	7	6	8
Small masses	1	5	3
Temperature 99° F. (or more)	8	9	8

Table X

ESTIMATED DURATION OF DISEASE BEFORE TREATMENT

	Group with initial leukopenia, months	Group with initially normal counts, months	Group with initial leukocytosis, months
Average before treatment	19.5	13.5	11
Longest before treatment	96.0*	60.0	48
Shortest before treatment	1.0	1.0	1

* The chronicity of one case of ninety-six months' duration gives a false impression concerning the duration before treatment. Disregarding that case, the average here would be thirteen months.

TABLE XI

DATE, TREATMENT AND TOTAL LEUKOCYTE COUNTS IN FOURTEEN CASES IN WHICH THERE WAS LEUKOPENIA BEFORE TREATMENT

Case	First Visit	Second Visit	Third Visit	Fourth Visit	Fifth Visit	Sixth Visit	Seventh Visit
7	10-22-29 4300 Rx*	11-15-29 6700 P.Rx†	12-13-29 4100 N.Rx	1-6-30 4800 Rx	2-11-30 1900 Rx	3-19-30 6900Rx	6-30-30 8000 N.Rx
8	3-17-30 4900 Rx	5-13-3– 3200 P.Rx	11-6-30 5200 Rx				
9	2-6-30 4600 Rx	3-3-30 2800 P.Rx	4-15-30 4500 N.Rx	9-8-30 3000 N.Rx	6-29-31 4900 N.Rx		
10	9-9-26 5000 Rx	10-5-26 Rx	12-16-26 Rx		5-24-27 5800 Rx		
11	7-29-24 3900 Rx	Rx			3-30-26 5900		7-20-26 4400
12	5-15-30 5300 Rx	6-24-30 4600					
13	8-30-30 4100 Rx	9-29-30 2600 P.Rx	11-3-30 4000 Rx	2-3-31 5200 Rx			
14	3-3-30 4700 Rx	4-7-30 P.Rx		12-8-30 3025 (sent in)			
15	10-30-30 4900 Rx	12-9-30 3800 Rx	1-27-31 4000 N.Rx	1-11-32 4500 Rx			
16	7-2-30 4400 Rx	N.Rx‡		12-11-30 6300			
17	12-26-30 4000 Rx	1-19-31 4000					
18	7-23-28 4400 Rx	Rx	Rx	Rx	Rx	Rx	3-14-31 7650 (sent in)
19	8-4-21 5400 Rx		11-29-21 6200 Rx	3-28-22 Rx	7-26-22 Rx		6-7-27 7800
20	2-4-29 5900 Rx	3-20-29 P.Rx	4-23-29 1900 P.Rx	10-23-29 6300			
Average count	4700	3957	4270	4732	4625	6900	6962

* Rx = complete treatment.
† P. Rx = partial treatment.
‡ N. Rx = no treatment.

TABLE XII

DATE, TREATMENT AND TOTAL LEUKOCYTE COUNT IN GROUP IN WHICH COUNTS WERE NORMAL BEFORE TREATMENT

Case	First Visit	Second Visit	Third Visit	Fourth Visit	Fifth Visit	Sixth Visit	Seventh Visit
26	2-19-27 7800 Rx*	3-29-27 6300 Rx					
27	5-19-26 8700 Rx	6-23-26 5400 Rx					
28	9-19-29 6700 Rx	10-21-29 Rx	12-5-29 5700 Rx	2-10-30 8000	8-28-30 6200	12-29-30 8200	11-30-31 4100
29	10-1-30 8600 Rx	10-25-30 5500 N.Rx†					
30	3-16-25 8400 Rx	5-11-25 Rx		11-13-25 6100			
31	5-1-26 6100 Rx	5-31-26 Rx		12-29-27 6200		10-9-28 4200	
32	7-15-29 9200 Rx	8-26-29 1200 P.Rx‡					
33	11-26-27 8800 Rx	12-16-27 2500 N.Rx	1-17-28 7300	2-7-28 20,800			
34	9-3-28 6200 Rx				6-24-29 5400		
35	2-14-27 7000 Rx	3-17-27 4000 Rx	4-20-27 3800 Rx	8-10-27 5700		8-18-28 6200	
36	5-26-27 6600 Rx		8-24-27 3200 P.Rx				
37	6-12-28 7700 Rx	7-16-28 Rx		1-24-30 9000			
38	11-2-28 7400 Rx	12-26-28 6000 Rx					
39	1-30-28 8200 Rx	2-21-28 Rx	5-1-28 6900			1-3-29 7000	
40	2-20-28 7100 Rx	4-11-28 4500 P.Rx	11-17-28 5500 Rx	10-8-29 5800 Rx	3-3-30 3900	5-22-30 6000	8-12-30 5000
41	8-20-28 8100 Rx	9-24-28 4500 Rx		4-25-29 5100			

* Rx = complete treatment.
† N. Rx = no treatment.
‡ P. Rx = partial treatment.

TABLE XII—(*Continued*)

42	7-2-30 6100 Rx	7-25-30 5600 N.Rx					
43	6-14-26 7100 Rx	7-12-26 7800 Rx					
44	2-17-26 7500 Rx	3-16-26 Rx	4-19-26 5200 Rx				
45	6-13-21 8400 Rx	Rx	10-18-21 2500		3-14-22 5200	11-24-26 7500	7-18-28 5700
Average count	7505	5827	5012	8337	5175	6515	5000

this group. In 14 cases, more than one count was made; Table XI indicates the dates of the counts and the number of leukocytes. For comparison, the 20 cases of the initially normal group and the 20 cases of the group with initial leukocytosis are analyzed in the same way. The references in Tables XI, XII and XIII to partial and complete treatment indicate roughly the areas treated. As has been stated, complete treatment consists of irradiation of all areas in which lymph nodes are prone to be enlarged. Partial treatment consists of irradiation only to those areas where enlargement of nodes can be demonstrated. In Table XI are recorded, for the group with initial leukopenia, the leukocyte count on admission, with subsequent leukocyte counts, whether or not treatment was given. Tables XII and XIII present these data for the initially normal group and the group with initial leukocytosis, respectively.

COMMENT

The average differential leukocyte count, before treatment, of the three groups under consideration, indicates the presence of a normal percentage of lymphocytes in the cases with initial leukopenia, with a diminishing percentage as the total leukocyte count increases to normal or above. On the other hand, the percentage of the polymorphonuclear leukocytes increases as the total leukocyte count rises, as is shown by comparison of the average differential count, before treatment, of the three groups (Table XIV). Other than the lymphocytes and polymorphonuclear neutrophiles, there is little variation, unless the presence of 5 per cent transitionals is considered of some importance. Bunting and others have indicated that a high leukocyte count, with lymphopenia and a high percentage of neutrophiles, might be interpreted as signifying that the disease had been present for more than a year. The results given here would indicate that there is no relation between the onset and the leukocyte count. One finding is obvious, that as the total number of leukocytes increases, the percentage of polymorphonuclear neutrophiles frequently increases, while the percentage of lymphocytes decreases proportionately, regardless of the duration of the disease. Eosinophilia was present in the group with initial leukopenia in percentage greater than 5 in 5 cases, the highest being 16 per cent, the second highest 8.5 per cent. The highest percentage of transitional cells was 9, in several cases it was 6 per cent. Large mononuclear cells were increased to 7.5 per cent in one case; in another case they were 5.5 per cent; in the remainder the proportion was less than 5 per cent. Among the patients with initially normal counts, the highest percentage of transitional cells was 8.5; in another

TABLE XIII

DATE, TREATMENT AND TOTAL LEUKOCYTE COUNT IN CASES IN WHICH THERE WAS LEUKOCYTOSIS BEFORE TREATMENT

Case	First Visit	Second Visit	Third Visit	Fourth Visit	Fifth Visit	Sixth Visit	Seventh Visit	Eighth Visit
46	8-5-24 19,300 Rx*	9-17-24 4800 Rx	10-14-24 4300 Rx	12-16-24 7100 Rx	2-23-25 8400	4-28-25 7300	9-28-25 8300	4-26-26 10,900
47	1-22-27 15,200 Rx	3-30-27 7600 P.Rx‡	5-3-27 9000 Rx	9-8-27 7900				
48	7-28-28 15,400 Rx	9-17-28 8200 Rx						
49	8-30-28 11,000 Rx	10-2-28 2700 Rx						
50	2-2-28 12,000 Rx	4-23-28 6200 P.Rx	7-4-28 8300 Rx	9-3-28 9300 Rx	12-24-28 7700	3-14-29 8700	12-4-29 13,700	3-12-30 19,000
51	2-12-27 29,700 Rx	3-15-27 Rx	4-16-27 Rx	6-0-27 Rx	10-18-27 19,200	12-28-27 19,500	6-20-28 11,000	12-10-29 22,500
52	2-21-28 10,700 Rx	3-28-28 8800 Rx	5-14-28 8900 Rx	6-22-28 11,000				
53	2-16-26 23,100 Rx	3-15-26 5200 Rx	5-18-26 Rx	7-18-27 10,000		10-16-29 8000		
54	3-20-28 18,800 Rx	4-16-28 7100 Rx	5-22-28 5800 Rx	7-25-28 5900	10-19-28 5000	12-5-28 4900	3-1-29 5000 N.Rx	4-9-30 7700 N.Rx
55	7-14-25 15,100 Rx	9-9-25 10,800 Rx	11-16-25 6600 N.Rx†		5-5-26 9000	1-10-27 10,200	2-17-27 7900	7-12-27 7700
56	7-29-27 13,200 Rx	Rx	12-8-27 7900 Rx	5-16-28 7900 Rx	6-12-28 5000	7-20-28 6600		
57	8-31-27 14,400 Rx	10-10-27 7400 Rx						
58	8-16-26 15,000 Rx	9-15-26 7300 Rx		2-4-27 8900		6-9-27 10,900		
59	3-18-30 12,600 Rx	4-21-30 3900 Rx		8-1-30 10,300 Rx	10-23-30 6100			
60	11-23-26 16,900 Rx	10-16-28 10,200 Rx						
61	12-5-29 14,300 Rx			7-3-30 11,800 Rx	8-13-30 11,200 Rx	2-24-31 14,500		
62	1-15-29 24,000 Rx	2-7-29 7300						
63	10-20-25 13,900 Rx	1-19-26 Rx		5 more Rx		8-16-29 5100	8-15-30 3400	
64	8-26-30 16,500 Rx	9-5-30 5500						
65	8-20-27 10,300 Rx	9-18-27 Rx	11-15-27 12,400					
Average count	16,070	6866	7900	9000	8950	9570	8200	13,560

* Rx = complete treatment.
† N. Rx = no treatment.
‡ P. Rx = partial treatment.

TABLE XIV

AVERAGE DIFFERENTIAL COUNTS BEFORE TREATMENT

	Lymphocytes, per cent	Polymorphonuclear neutrophiles, per cent	Transitionals,* per cent	Eosinophiles, per cent	Basophiles, per cent	Large mononuclears,* per cent
Initial leukopenia	26.2	63.7	3.1	3.8	0.4	2.6
Initially normal count	22.4	68.8	5.0	2.6	0.6	2.2
Initial leukocytosis	14.9	77.3	2.2	3.7	0.3	1.7

* These two groups, the transitionals and large mononuclears, are more properly placed together under the heading monocytes.

case the percentage was 6. Eosinophilia of 7.5 per cent was present in one case, of 7 per cent in another. The proportion of large mononuclear cells was 6 per cent in only one case. In the group with initial leukocytosis, the only variation of significance was the presence in one case of 42 per cent eosinophile cells; in all the other cases the percentage was 5 or less. All of these are isolated cases, and are mentioned only because various authors have attached considerable importance to similar cases.

After irradiation, the total leukocyte count fluctuated considerably. Table XI indicates the date of treatment, the leukocyte count and the treatment (partial, complete or none) of the group with initial leukopenia. By arranging the counts in order, so that the date of the first visit is in one line, the second visit in another, and so forth, it is possible to strike an average. Thus, the leukocyte count of 14 patients with initial leukopenia, whose subsequent blood counts are recorded, averaged 4,700 on their first visit, before any treatment had been given. In every instance, roentgen therapy was given. Approximately four weeks later, the patients returned, at which time the average leukocyte count (7 available) was 3,957 (a loss of 16 per cent). In one case a gain of 2,400 cells was noted; in another, the count had returned to a level corresponding with that before treatment. In all cases employed in arriving at the averages, either partial or complete treatment was given. In the same way, the available data for the third visit were averaged; the leukocyte count was 4,270, or a loss of only 9.9 per cent, from the original count. Two patients had higher leukocyte counts at the third visit than before the first treatment; 3 had approximately the same counts; the remainder had lower counts. The data beyond the third visit are extremely varied and would hardly permit generalization. Specific instances having interest are Cases

TABLE XV

AVERAGE TOTAL LEUKOCYTE COUNT AND THE PERCENTAGE LOSS IN THE THREE GROUPS AFTER IRRADIATION AT SECOND AND THIRD VISITS (FOUR AND EIGHT WEEKS AFTER TREATMENT)

Visit	Group with initial leukopenia		Group with initially normal counts		Group with initial leukocytosis	
	Leukocytes for each cu. mm. of blood	Loss, per cent	Leukocytes for each cu. mm. of blood	Loss, per cent	Leukocytes for each cu. mm. of blood	Loss, per cent
First	4700		7505		16,070	
Second	3957	16.0	5827	22.4	6,866	58.6
Third	4270	9.9	5012	33.3	7,900	50.9

TABLE XVI

DIFFERENTIAL COUNT BEFORE AND AFTER TREATMENT IN GROUP WITH INITIAL LEUKOCYTOSIS

	Lymphocytes, per cent	Polymorphonuclear neutrophiles, per cent	Transitionals, per cent	Eosinophiles, per cent	Basophiles, per cent	Large mononuclears, per cent
Before the first treatment	14.9	77.3	2.2	3.7	0.3	1.7
Four weeks after the first treatment	19.7	68.8	4.5	2.3	0.4	4.3

7 and 20 in which there was marked leukopenia (1,900). Partial cautious treatment was given in each of these two instances and a month later the counts had risen to 6,900 in Case 7 and six months later to 6,300 in Case 20. It may be objected that four weeks after treatment the leukocyte count should be well on the return to its level before treatment. It is evident, however, that much injury to the blood was not done by the doses used in the cases recorded in Table XI, since all of the patients were markedly benefited. An increase instead of a decrease of the total number of leukocytes occurred in occasional cases. Case 17 was complicated by the presence of severe infection of the diseased nodes. Immediately after irradiation, the leukocyte count increased from 4,000 to 5,000. Eight days later it was 5,200, and three weeks after treatment it fell to 4,000, which was the level before treatment. This case may be somewhat exceptional, but a temporary and transitory increase has frequently been reported in the literature, particularly with small doses. The differential count varied only slightly.

The group with initially normal counts (Table XII) was analyzed in the same manner. The leukocyte count averaged 22.4 per cent less than before treatment, and 33.33 per cent less at the third visit.

A study of the changes in the third group, that composed of patients with ini-

TABLE XVII

COMPARISON OF DURATION OF DISEASE IN THREE GROUPS

	Group with initial leukopenia	Group with initially normal counts	Group with initial leukocytosis
Dead	6	12	13
Average duration of disease of those who are dead, months	42.66*	31.16	35
Living	13	8	7
Average duration of disease until patient last heard from, months	35	31.6	36

* The presence of one chronic case has made this figure very high. If this case is excluded, the average would be 34.11 months.

TABLE XVIII

STATISTICS ON DURATION OF THE DISEASE IN THE THREE GROUPS

	Group with initial leukopenia, months	Group with initially normal counts, months	Group with initial leukocytosis, months
Before treatment	19.5*	13.5	11.0
After treatment	22.1	18.3	25.0
Total†	41.9‡	31.3	35.9

* See note, Table x. More than thirteen months would be more nearly an average.

† Total: Duration from known onset until either death or last heard from.

‡ One patient, whose disease lasted eleven years, makes this appear unreasonable. Without including this case, the figure should be thirty-four months.

tial leukocytosis (Table XIII) is most interesting. The average before treatment, 16,070 cells, was reduced to 6,866 cells, or 58.6 per cent less at the second visit, and had recovered only to a slight extent at the time of the third visit, when the average count was 7,900, even though partial or complete treatment was given in each instance.

Table XV is a basis for correlation studies of the average leukocyte counts in the three groups, showing the number of cells and percentage loss four and eight weeks after the first treatment.

A comparison of the average differential counts in the group with leukocytosis, before the first treatment and four weeks after the first treatment, shows that the most marked destruction involved the polymorphonuclear leukocytes, both in percentage and absolute numbers (Table XVI).

It is generally admitted that lymphocytes are much more sensitive to roentgen and radium rays than are the polymorphonuclear neutrophiles, and it is difficult to explain this apparent inconsistency. It has been suggested that the neutrophiles are immature, or at least that younger forms are present in the blood stream, from excitation of the bone marrow by the disease process. A marked increase in leukocytes is also characteristic of leukemia, although the particular cell involved is either lymphogenous or myelocytic in origin. Irradiation produces a marked beneficial result in leukemia, and simultaneous with the remission, lowering of the leukocyte count occurs. It is possible that some of the cells in the blood stream of patients who have Hodgkin's disease or lymphosarcoma are variations from the normal, or are obviously too numerous, which indicates a similarity to leukemia. It seems, also, that if the leukocytes are numerous, treatment by roentgen rays causes a greater percentage loss than when the total leukocyte count is low. This does not confirm the observations of Stetson, who, in a group of patients suffering from diseases other than blood dyscrasia, noted a 39 per cent loss among patients who initially had low leukocyte counts and only 13 per cent loss among those who initially had high leukocyte counts.

A comparison between the ultimate results in terms of duration of the disease, either from time of onset or from time of first roentgen treatment until death, or until last heard from, is not unfavorable to patients with leukopenia. Table XVII gives the impression that the largest number of dead is in the group with leukocytosis, but this is not a correct impression, since the dates of registration of patients with initially normal leukocyte counts and of patients with initial leukocytosis were generally several years earlier than of patients with initial leukopenia. This may also give a false idea of the total duration of the disease among those living who had initial leukopenia. However, a series of this type, with the onset so problematic, can show only that initial leukopenia is not a contraindication to conservative and cautious irradiation and is of no definite prognostic significance as far as length of life is concerned. If leukopenia has any prognostic significance at all, it would seem slightly favorable rather than unfavorable. Table XVIII shows the average duration of the disease in the three groups, before the first treatment and subsequently until the patient died or was last heard from.

CONCLUSIONS

1. In lymphoblastoma, as defined, leukopenia is not common. Its incidence was 5.5 per cent in the group of 450 cases studied. When it is present, the differential leukocyte count appears normal.

2. The presence of initial leukopenia in this group of diseases could not be recognized without a leukocyte count because they were not accompanied by any recognizable clinical signs. Sex, age, pathologic diagnosis, size and distribution of the enlarged nodes, as well as the duration of the disease, did not yield a characteristic vari-

ation from the group of patients with normal initial counts and from those with initial leukocytosis.

3. From this study, leukopenia does not have any prognostic significance.

4. Leukopenia in lymphoblastoma is not a contraindication to roentgen therapy.

5. Cautious, conservative roentgen therapy, as described, can be given without incurring risk, and yet brings about beneficial results.

6. Initially normal leukocyte counts (between 5,500 and 10,000) occurred in 58.5 per cent of the series of 450 cases; a count of more than 10,000 in 36 per cent. The higher the initial leukocyte count, the higher was the percentage of polymorphonuclear neutrophiles noted in most instances, as well as a proportional lymphopenia.

7. The loss of leukocytes after irradiation in a group in which the initial leukocyte count was low averaged 16 per cent and 9.9 per cent respectively, four and eight weeks after the first irradiation. In the group with normal initial counts, the percentage loss was 22.4 per cent and 33.3 per cent. In the group with initial leukocytosis, the loss was 58.6 per cent and 50.9 per cent. In the last group, the loss was due to destruction of polymorphonuclear neutrophiles rather than of lymphocytes, the explanation of which is obscure and deserves further study.

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CERVICAL LYMPH NODES IN INTRAORAL CARCINOMA: SURGERY OR IRRADIATION?*

By JAMES J. DUFFY, M.A., M.D., F.A.C.S.
Memorial Hospital
NEW YORK CITY

THE method of treatment of cervical lymph nodes in intraoral carcinoma has been changing over a period of years. The treatment up to the time of Butlin in 1895 seems to us now to have been rather haphazard. Butlin advocated what we now designate as a partial dissection of the neck—en bloc removal of the tissues of the anterior triangle of the neck on the side of the primary lesion. This procedure was advised whether or not metastatic nodes were palpable, and was based on the hypothesis that the successful treatment of intraoral cancer depended as much on the care of the cervical lymphatic region as on the treatment of the primary lesion. When the results were not as good as anticipated, the surgical approach was amplified, first by complete unilateral dissection and later by dissection of the nodes of both sides of the neck. Complete unilateral or bilateral neck dissection has been the method of procedure in most surgical clinics for over twenty-five years, and has been applied to all cases, whether nodes were absent, or present and operable, or in an advanced stage of disease.

During this period the only major variation in the surgical treatment of intraoral cancer has been the sequence in which the primary lesion and the regional nodes have been cared for; that is, whether the excision of the primary growth has been done first and followed immediately or within a few days by the neck dissection, or whether the excision of the cervical nodes has preceded the removal of the primary lesion. There is no reason why the latter method should be followed. The lymph nodes serve as a protective barrier to the spread of cancer, and if these are first to be excised, any cell emboli that may be set free during the interval between the surgical procedures, or at the time of removal of the primary growth, may be deposited in areas where there is no growth restraint; or the metastatic emboli may escape to more distant locations where they are completely beyond surgical excision or adequate irradiation.

Since the introduction of radium and roentgen rays into the field of cancer therapy, the trend, in many clinics, has been away from routine surgery toward radiation treatment of the cervical region. In the earlier days this change of procedure was stimulated by the description of the transitional cell carcinoma and lympho-epithelioma, by Ewing, and Regaud and Schmencke, and then by the grading of tumors by Broders.

During the past few years the trend in the treatment of the cervical region has been the further limitation of surgery and in many places there has been an elimination of radical surgery in this region, so that we are approaching the stage where the radiation treatment is becoming too radical to the exclusion of surgery. As more knowledge and greater familiarity with the physical agents are attained, the radiation treatment of the neck may be the method of choice, but this should be ascertained more gradually by first applying it to the inoperable and borderline cases. As the results in these types of cases improve, then the method may be extended to the operable group. At the present time, surgery of the cervical region in all types of intraoral cancer cannot be discarded in favor of irradiation. Nor can the surgeons disregard radiation therapy of the neck in certain types of intraoral carcinoma. A narrow point of view will only serve to discredit that method which is overdone to the ex-

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clusion of the other procedure. This seems especially applicable to radiotherapy at the present time. Radiotherapists are now including all types and stages of metastatic disease of the cervical region in their field of therapy. There was a time, also, when surgeons attempted to eradicate metastatic disease that was technically and totally inoperable.

In a discussion of operability of cervical nodes, the classification usually depends on technical operability alone, whereas other manifestations should be considered. The present analysis and discussion include these other factors, and the presentation may apparently emphasize the indications for surgery; however, it is with the understanding that a contraindication to the surgical treatment is an indication for an irradiation program of treatment, except, of course, in the advanced case in which no treatment is indicated. Radiotherapists too often undertake the treatment of the very advanced lesions as surgeons too often attempt to dissect the cervical nodes when these have reached an inoperable stage of development. Ill-advised irradiation undoubtedly causes more actual pain to a patient with a hopelessly advanced metastatic lesion than an improperly planned neck dissection in an unsuitable case.

When a patient with intraoral cancer is admitted to the hospital, one of three conditions is presented in the cervical region. Either there are no palpable metastatic nodes of the neck, or the nodes are present, but operable, or the disease in the lymphatic system has so far progressed that it is beyond the scope of surgery. This classification is based on the purely surgical aspect and it does not take into consideration the grade of malignancy of the primary tumor, its extent, and other manifestations, which are very important factors and will be discussed later.

The absence of palpable nodes means there are presumably no metastatic nodes. It is very common to find lymphadenitis due to an infected ulcerative primary lesion. The clinical diagnosis is made by the consistence of the node, that is, whether it is soft, firm or hard; but repeated palpation of the cervical region during the course of the treatment of the primary lesion is most valuable, because an inflammatory node may be tender and may vary in size, usually diminishing as the intraoral infection decreases and it is fully movable, whereas a metastatic node is hard, gradually increases in size and is not tender. Aspiration biopsy, though not infallible, will differentiate a metastatic from an inflammatory node in a fair percentage of cases. The absence of cancer in an aspiration biopsy, however, is never conclusive.

Following is the outline of the indications and contraindications for neck dissection. For a case to be operable all the indications must be present. Any one contraindication completely excludes radical neck dissection.

Neck Dissection

Indicated	Contraindicated
1. Primary lesion is controlled.	1. Primary lesion is uncontrolled.
2. Primary lesion is limited to one side of oral cavity.	2. Primary lesion extends to or beyond the midline of oral cavity.
3. Primary lesion is shown to be of highly differentiated cell type.	3. Primary lesion is shown to be of undifferentiated cell type.
4. Cervical metastases are present and limited to one group of nodes or nodes in two contiguous cervical triangles.	4. No metastatic nodes are present.
5. Capsule of nodes is not infiltrated by carcinoma.	5. Capsule of node is infiltrated by carcinoma.
6. Opposite side of neck is free of metastases.	6. Cross or bilateral cervical metastases are present.
7. No distant metastases are present.	7. Distant metastases are present.
8. Patient is in good general condition.	8. Patient is in poor general condition.

Having expressed these criteria, they will be discussed individually, the basis being 252 cases of carcinoma of the lateral border of the tongue treated at Memorial Hospital during the years 1923–1931, inclusive. Carcinoma of this region was selected because these lesions are capable of producing all the conditions and manifestations heretofore mentioned in the indications and contraindications for neck dissection:

(1) Carcinoma of the lateral border of the tongue is too often uncontrollable; (2) it may involve only one side of the tongue and be very limited or may extend beyond

the median raphe and involve much of the organ; (3) the histologic gradation varies from Grade 1 to the more malignant Grade 3, classified as radiosensitive; (4) the cervical region may have no metastatic nodes or a very limited number of metastatic nodes; (5) is often in an advanced stage, the disease having perforated the node capsule or having infiltrated all the structures of the cervical region; (6) contralateral or bilateral metastatic nodes are frequently present in late cases and occasionally in otherwise early cases; (7) carcinoma of the lateral border of the tongue may give rise to distant metastatic deposits; (8) the disease occurs in the usual decades, and is therefore much more frequent in the latter years of life, when patients are subject to many maladies, especially of the heart, blood vessels and kidneys.

1. *Controllability of Primary Lesion.* In this series of 252 cases of carcinoma of the lateral border of the tongue, 18 patients died of intercurrent disease or were lost before it could be ascertained whether or not the primary disease could be controlled. Of the 234 cases who survived for varying periods of time which seemed adequate to make some estimate of the primary lesion, in 62.3 per cent the disease was apparently controlled and in 37.7 per cent it was uncontrolled. Of the controlled cases, some patients have remained well five years and more, many have died of local or distant metastases, or intercurrent disease. Of the other 88 patients showing uncontrolled disease (37.7 per cent) many have died,—some with only local persistence of the disease, but most of them with both primary and secondary disease. One living patient now has disease present, but it is questionable whether it is persistent disease or another lesion, so that the previous lesion might be classified as controlled. However, this case is rated in these statistics as a failure to control the primary disease.

The cases that were uncontrolled were not limited to the advanced primary lesions. Of these 88 uncontrolled primary lesions, 51 were in an advanced stage of development, and 37 would be considered early or borderline. This estimate is on the basis of clinical judgment, whether the lesion was extensive, involving much of the tongue or adjacent mucosa of the mouth, or whether the growth was limited to a portion of the tongue, roughly within 5 to 6 cubic centimeters in volume. It is to be noted that 58 per cent of the uncontrolled lesions were advanced primary lesions. Therefore, a neck dissection is not indicated when the oral lesion is advanced, until the primary disease is entirely eradicated. Since 42 per cent of the early primary lesions persist in spite of treatment, it is more advisable to delay surgical care of the cervical region until there is an assurance that the primary lesion is controlled. This required interval of time may be devoted to moderate external irradiation, thereby obtaining some growth restraint, but not damaging normal tissue to the extent that neck dissection will be impossible.

It should be noted that not all patients with the uncontrolled primary lesion died. In this uncontrolled class were included not only those cases which showed persistent disease to death, but also those cases in which a partial glossectomy was indicated for infection or fibrosis, or both, and in which the microscopic appearance of the tissue removed indicated that cancer cells were still viable. From this survey it must be concluded that radical surgery of the cervical region should be delayed until the primary lesion is apparently controlled.

2. *Extent of Primary Lesion.* If the primary lesion involves both sides of the oral cavity (except lesions of the lip, if these are included in the oral group), a neck dissection is not indicated. Such involvement may be observed in central lesions, such as those in the base of tongue or in the soft palate, or the lesion may originate on one side and extend to the opposite side, as is frequently noted in carcinoma of the lateral border of the tongue.

In this series of cases, the extension of the primary disease beyond the midline of the oral cavity was observed in over 20 per

cent of the cases, in the more advanced cases usually with extensive unilateral or bilateral cervical metastases.

When this disease has extended to or beyond the midline, the metastatic nodes have usually reached a stage of development well beyond operability. If there is only unilateral palpable involvement of nodes, it is quite likely that when the primary disease has so far extended that the opposite side of the organ is involved, metastases will be manifest soon in the other side of the neck; but surgical excision is contraindicated for other reasons: first, it is unlikely that the primary lesion can be controlled, and second, bilateral neck dissection has rarely eradicated bilateral metastatic disease. The mortality from bilateral neck dissection would most likely exceed the number of cases cured by bilateral neck dissection. There are no available statistics to prove this contention, but the mortality from bilateral dissection of the neck cannot be ignored. If the disease from the extended lesion has not been deposited in the second side of the neck, there is no need for the bilateral dissection, and if it has so metastasized, the mortality percentage from the surgical procedure will quite surely surpass the percentage of cure.

The percentage cure of carcinoma of the base of the tongue is extremely small, when the metastatic cervical nodes are subjected to surgical excision. This holds even though in many cases the cells of the growth are well differentiated. Many cancers in this region are so graded. The poor results in lesions of the base of the tongue are due to the midline position of many of these growths, with consequent metastases to both sides of the neck as well as to the mediastinal lymph nodes.

3. *Grade of Primary Lesion.* It is not necessary to dwell long on the criteria for neck dissection as related to the malignancy of the oral tumor. Before the degrees of malignancy were understood, the very prompt and widespread recurrence after neck dissection of carcinoma in the operative wound was the source of considerable consternation. This manifestation usually occurs within a few months of the surgical procedure and is not confined to any one portion of the neck, but the growth invades the skin about the scar and often infiltrates the skin to the full extent of the flaps made to expose the structures of the cervical region. This type of infiltrative growth promptly ulcerates, and because there is also recurrence in deeper regions of the neck, hemorrhage frequently occurs, from early ulceration and erosion of some one of the many blood vessels. Although the bleeding from the lesser vessels may be controlled by moderate pressure, the constantly associated infection increases the ulceration until there is massive necrosis of the tissues of the neck with hemorrhage from the larger blood vessels, which cannot be controlled. The depletion of the patient by repeated bleeding from the erosion of even the smaller vessels decreases his resistance to bacterial infection, so that death intervenes, caused by infection as much as by carcinoma. This sequence of progressive disease is most common in the transitional cell type of carcinoma and lympho-epithelioma, and to a lesser extent in epidermoid carcinoma, Grade 3. The first two types seldom occur in the lateral border of the tongue, being much more frequent in the base of the tongue, the tonsil and the nasopharynx. The same sequence of recurrence—infiltration, ulceration, with erosion of the cervical vessels —may and does occur in the more adult types of carcinoma, when ill advised or inadequate surgery is done.

In this group of 252 cases of carcinoma of the lateral border of the tongue, 21 per cent were classified as Grade 1; 76 per cent as Grade 2; and 3 per cent as Grade 3. There was none of the transitional cell type or lympho-epithelioma in this region of the tongue, these types being limited to the base of the tongue, where 20.4 per cent of a representative group recently analyzed were either transitional cell carcinoma or lympho-epithelioma. This type of cell as

well as central location of the lesion accounts in some measure for the poor results in the surgical treatment of metastatic nodes from carcinoma of the base of the tongue, because these types metastasize early and bilaterally, frequently giving rise to distant metastases in the mediastinum, abdominal cavity and in bone. The following table gives the percentages of the various grades of carcinoma in the different portions of the tongue and the location of the metastases.

TABLE I

GRADE OF TUMOR AND LOCATION OF METASTASES

Carcinoma of the Tongue

Location of Lesions	Grade of Tumor				Location of Metastases						
	Grade 1	Grade 2	Grade 3	Transitional and Lympho-epithelioma	Submental nodes	Submaxillary nodes	Upper deep cervical nodes	Carotid nodes	Nodes on opposite side of neck	Bilateral nodes	Distant metastases (Clinical findings)
Tip of tongue	28.5%	57.2%	14.4%	0	5.3%	31.6%	5.3%	26.4%	10.5%	20.9%	0
Dorsum of tongue	56.2%	37.5%	6.2%	0	0	6.8%	59.6%	13.5%	0	20.1%	0
Lateral border of tongue	21%	76%	3%	0	0	31.5%	20%	37.1%	0	11.4%	2.6%
Base of tongue	4%	66%	9.5%	20.4%	0	1.3%	53%	24.7%	0	21%	4.9%

4A. *Limitation of Cervical Metastases.* The fourth in the group of criteria for neck dissection in oral carcinoma will necessarily be considered under two headings, because the indication and contraindication are not antitheses as in the other criteria, which were discussed together. Therefore, the lesions of the lateral border of the tongue will be used for the indications, and this same group together with a larger group of all oral lesions, previously reported, will be used to explain the contraindications for neck dissection.

The condition of the cervical region is classified, irrespective of the primary lesion, in four groups: (*a*) no metastatic nodes throughout the course of the disease; (*b*) developing metastatic nodes; (*c*) admitted with operable nodes; (*d*) admitted with inoperable metastatic nodes. The cases have been classified according to the criteria previously enumerated, except in regard to the grade of the tumor. The futility of neck dissection in the more malignant types of cancer was not fully understood in 1923, the first year included in these statistics. At that time the classification as to operability was based solely on the technical operability of the cervical region. The gold tubes for the interstitial application of radon into the tumor mass had not been developed at that time. These were first used extensively in 1925. As gold tubes of radon were not used in the earlier years, and underdosage by external irradiation, as we now understand dosage, was the rule, an occasional case was subjected to surgical removal of the nodes which would now be assigned to radiation therapy only. Otherwise the criteria have held throughout this group of 252 cases of can-

cer of the lateral border of the tongue. Before comparing the efficacy of surgery and irradiation of the operable group, it might be well to enumerate the number of cases in the four classes into which the cases are divided according to the condition of the neck (Table II).

TABLE II

CERVICAL LYMPH NODES IN 252 CONSECUTIVE CASES OF CARCINOMA OF LATERAL BORDER OF TONGUE

Years 1923 to 1931 incl.	Total Cases	No Nodes Throughout	Developed Nodes		Admitted with Operable Nodes	Admitted with Inoperable Nodes
			Operable	Inoperable		
	252	103	48	23	37	41

In this group of 85 cases which had operable nodes on admission or developed nodes after admission, almost equal numbers were subjected to surgery of the cervical region and to radiation treatment of the nodes. The surgical cases had microscopic proof of the metastases in all instances, but some of the irradiation cases lacked this proof while the others had an incisional or aspiration biopsy. It is not necessary to give the percentages here, because in all cases the clinical evidence seemed quite adequate. Assuming that all irradiation cases had metastatic carcinoma, even then the comparative figures should be conclusive in regard to the procedure to be followed.

Forty-four patients were treated by irradiation, and in 41 cases a neck dissection was done. The cases for these methods were not at all times deliberately chosen. In most instances, in which radiation therapy was used, the patient refused operation. Rarely some other disease contraindicated radical surgery and a few were purposely allotted to radiation therapy.

The neck dissection in practically all the surgical cases was a radical dissection. In the first year or two covered by the statistics, in an occasional case a lesser procedure was done—removal of tissue of one or two triangles of the neck. At no time was a simple excision of nodes done.

Of the 44 cases of operable neck metastases, subjected to irradiation, 4 remained free of disease for five or more years. Two of these had positive biopsies at the time of the surgical exposure for radon implantation. The diagnosis in the other 2 cases depended on clinical examination. The group so treated, therefore, had a five year survival of 9.1 per cent.

In the operable group in which a neck dissection was done in 41 cases, 8 patients, or 19.5 per cent, are known to have survived for five years or more. In the total operable group were 2 cases lost at four and four and a half years, both free of disease at the time, and both had proved metastases in the cervical region. It is most unlikely that there would be a recurrence at such a late date. Though such an event might occur in lip carcinoma, it is not so in carcinoma of the tongue. There was 1 case each in the surgically treated and radiation treated groups. If these cases are added to their respective groups, the percentage survival of the operable and irradiated group is 11.4 per cent, and of the surgically treated group it is 21.9 per cent. These percentage figures show considerable difference in the results of irradiation and surgery in the operable group. To get the proper estimate, these figures should be compared with each other. In so doing, it is learned that the surgical cases showed a better result by nearly 100 per cent, even though there were included in the radiation group 2 cases that were not proved to have metastatic carcinoma microscopically, although the clinical evidence seemed sufficient to classify the nodes as metastatic nodes. If the non-proved cases were deleted from the statistics, the percentage of cured cases in the irradiation group would be 6.9 per cent, whereas the surgical group would remain the same—21.9 per cent. These latter two percentages include the four year and four and a half year cases. It might be main-

tained by the proponents of irradiation that the radiation treatment of the earlier cases was not as good as during the later years. That is granted. But because of the less efficacious irradiation by the roentgen ray and glass seeds of radon, some doubtful cases were subjected to surgery. These were included in operable and operated group, but would now be allotted to irradiation. It is certain that these would more than compensate for the less efficacious irradiation of that period. The analysis of these two groups of cases by years has not shown any marked difference in the percentages.

Although metastatic carcinoma of the neck can be cured by irradiation, as shown by the figures, the relative percentages of the irradiated and the operated cases in the operable group leave no doubt as to the method to be employed. It may be that further experience with the more protracted external irradiation and the more accurately estimated dosage by interstitial radon may improve the results in the irradiation group. This experience should be obtained not in the operable group, but in the large number of inoperable cases, many of which are only slightly beyond operability. As these results are improved, then the irradiation method may be extended to the operable cases. Moreover, there is always a small percentage of patients in the surgical group who refuse the radical surgery and these may be conscientiously treated by irradiation.

If the mortality of neck dissection were high, then there might be some hesitancy in its undertaking. In ascertaining the percentage mortality, to the above series of 41 operable and operated cases there must be added 9 cases in which neck dissection was done for supposed operable nodes, but microscopic examination proved the nodes to be inflammatory; therefore these cases are classified as having had no nodes throughout. In this total series of 50 neck dissections there was one death, a mortality rate of 2 per cent. This patient died of pneumonia, but he had a partial glossectomy at same time the neck dissection was done. It is reasonable to attribute the pulmonary infection to glossectomy rather than neck dissection. Nevertheless, it is classified as a fatality following neck dissection.

4B. *Absence of Cervical Metastases.* Because the contraindication to neck dissection in this criterion is not simply the opposite of the indication for neck dissection, it must be the subject for a distinct analysis.

If there are no nodes, a so-called prophylactic neck dissection is not indicated. The statistics which lead to this contraindication to dissection of the cervical region are taken from two sources,—the present series of cases of carcinoma of the lateral border of the tongue and a larger group of carcinomas of all the regions of the mouth, which was previously published in 1927. Time has not permitted the re-analysis of this large series. Moreover, there is no reason to believe that there would be much change in the percentages. It is quite probable that there would be fewer advanced cases as evidenced by cervical metastases, because the laity is becoming more cancer conscious, seeking advice earlier, and present-day treatment is more efficacious.

In this series of 252 cases of carcinoma of the lateral border of the tongue, 103, or 40.8 per cent, gave no evidence of regional lymph node involvement. Forty-eight patients admitted without metastatic nodes developed operable cancerous nodes during the period of observation, and 23 developed inoperable nodes in the cervical region. The number of patients developing inoperable metastatic nodes would suggest a so-called prophylactic neck dissection, if the figures were accepted without further analysis. However, in some of the cases developing inoperable nodes, the metastases occurred bilaterally, usually from advanced and extensive primary disease, which was uncontrolled and therefore, on that basis, contraindicated surgery even before the metastases manifested themselves. A few had distant metastases at the same time as the cervical metastases appeared and radi-

TABLE III

CONDITION OF CERVICAL REGION IN SERIES OF CASES OF ORAL CARCINOMA

Cervical nodes in 1,363 cases of intraoral cancer

Site of Primary Lesion	Total Cases	Percentage no Nodes Throughout	Percentage Operable Nodes	Percentage Inoperable Nodes	Percentage Developing Nodes
Lip	271	77.5	10.0	4.0	8.5
Tongue	268	43.3	13.0	14.5	28.7
Floor of Mouth	122	44.2	22.5	14.5	18.8
Inf. Maxilla	84	65.5	10.7	11.9	11.9
Sup. Maxilla	62	72.6	9.7	3.2	14.5
Hard palate	31	77.4	6.4	9.7	6.4
Soft palate	34	58.8	11.8	11.8	17.7
Buccal mucosa	98	60.2	13.3	11.2	15.3
Tonsil	124	32.3	25.0	22.1	12.5
Antrum	65	70.8	10.8	13.5	17.4
Larynx—int.	105	69.5	5.7	15.2	3.8
Larynx—ext.	99	44.4	11.1	41.4	3.0

cal surgery would have been of no avail. An appreciable number of cases were the highly malignant type and metastasized widely,—this highly malignant type is not amenable to surgery. An occasional patient declined to return for observation for a time, during which period an inoperable cervical metastasis occurred. In the last group some benefit might seem possible from a prophylactic neck dissection, but this possible benefit seems to have been nullified when the figures (Table II) are examined. To attain any possible cure in this extremely limited group, it would have necessitated a radical neck dissection on 211 patients, because surgery would have been done on the 103 cases with no metastatic nodes throughout the course of the disease, on the 71 patients developing metastatic nodes, and on the 37 cases that were admitted to the hospital with the cervical region in an operable condition. A neck dissection would not have helped the 103 patients who had no metastatic nodes at any time, nor would it have made any significant change in the result of those developing inoperable metastases. The routine neck dissection would mean this, that 211 would have had a radical neck dissection, whereas only 88 could reasonably have been expected to have derived any benefit. From this group were taken the 85 cases previously discussed under indications for surgery. One hundred twenty-three patients would have needlessly had a radical neck dissection. The mortality of this operation usually varies from 2 to 6 per cent. It is not reasonable to expect that the five year results would improve by such a percentage. To these figures may be added the thought that 123 patients would have suffered the physical and mental discomfort of a major operation, from which they obtained no benefit.

In 1927 I published the figures for a much larger group of cases of all the oral lesions.

Those figures show the number and percentage of the cases in regard to the condition of the cervical region for all the lesions of the oral cavity. From Table III are derived the figures shown in Table IV on the next page.

It is noted in this table that the lesions of the different regions of the mouth show varying percentages of freedom from cervical metastases. Several factors are responsible for this fact. Among these factors may be mentioned the mobility of the part involved, the number of lymph channels draining the part and especially the degree of malignancy with the proportionate num-

ber of highly malignant lesions of the several regions of the mouth. Comparing the figures for carcinoma of the lateral border of the tongue (Table II) the difference is not as great as it at first seems to be, because in Table IV all the regions of the tongue were included. The base of the tongue is notably likely to show early cervical metastases, especially because of the frequency of the highly malignant type of growth. To a lesser extent, these figures vary because in the larger group (Tables III and IV) the percentages were tabulated for a period of only two years, or less, if death from uncontrolled primary lesion or intercurrent disease intervened; whereas in the series of cases of carcinoma of the lateral border of the tongue, all cases were followed up to the time of death,—for five or more years in the cured cases.

TABLE IV

CASES ADMITTED WITH NO CERVICAL METASTASES AND THE PERCENTAGE FREEDOM FROM METASTASES

Primary	Cases Admitted without Nodes	No Nodes Throughout	Percentage of Cases with no Nodes on Entrance Which Did Not Have Nodes Throughout
Lip	233	210	90.1
Tongue	194	117	60.3
Floor of mouth	77	54	70.1
Inferior maxilla	65	55	84.6
Superior maxilla	54	45	84.3
Hard palate	26	24	92.3
Soft palate	26	20	77.0
Buccal mucosa	74	59	79.7
Tonsil	56	40	71.4
Antrum	54	46	85.2
Larynx—intrinsic	77	73	94.8
Larynx—extrinsic	47	43	91.5
Total	983	786	79.95

Analyzing the figures in Table III in the same manner as in Table II, the figures are important. There were 1,363 consecutive cases in the group analyzed for publication in 1927. Of these, 983, or 70 per cent, were admitted without palpable metastatic nodes; 175 patients had operable nodes; and 205 patients were admitted with inoperable nodes. If a neck dissection had been done on all cases except the inoperable group, there would have been 1,158 surgical operations on the cervical lymphatics, whereas only 372 patients had or developed operable nodes. The difference in these figures indicates the number of patients (786) on whom a major operation would have been done with little or no gain in the ultimate results.

5. *Infiltration of Nodal Capsule.* The criteria dealing with the carcinoma involving or perforating the capsule of the lymph node cannot be discussed on a statistical basis, because these cases have been assigned for treatment by irradiation. This has been so for many years, because it was very promptly learned that surgery in this class of cases was futile. The rapidly growing, and early metastasizing type involves the capsule early and surgery is contraindicated because of the degree of malignancy. Other local metastases as well as distant deposits are probably present, but not palpable at the time. The more differentiated types of carcinoma extend beyond the node capsule more slowly, but when the growth has so far progressed that it has invaded or perforated the capsule, the probability of eradicating the disease by surgery is most distant. Besides the possibility of more distant metastases and the uncontrollability of the primary lesion, there is the added difficulty of estimating the limits of the metastatic disease. The carcinoma has probably extended well beyond the palpable mass, often infiltrating an important blood vessel of the region, or involving the periosteum of the mandible if the metastasis is in the upper portion of the neck. Following the infiltration of the capsule, the carcinomatous nodes seem to necrose centrally very promptly, because of the interference with the blood supply. The cavity may be very irregular in contour, and may even involve the surrounding

structure, so that any surgical procedure will cause contamination of the normal tissue by viable cancer cells. Unsuspected involvement of the platysma muscle is often noted when exposing such a node for radon implantation. The extent of the growth in this more advanced stage of metastatic disease is impossible to ascertain. The sequence of events, following contamination of the operative field by viable cells from a node with perforated capsule, is the same as discussed under grade of the tumor, namely recurrence, infiltration of skin and other structures of the cervical region, erosion and hemorrhage. The only variation is the greater rapidity of the progress, because of the diffuse contamination.

A metastatic node that is irregular in outline, merges with surrounding tissue, and is partially or completely fixed, is not a suitable condition for radical surgery.

6. *Extent of Cervical Metastases.* Bilateral cervical metastases contraindicate neck dissection. Contralateral involvement is practically the same contraindication, because with contralateral metastases, the cervical region on the same side as the primary lesion quite certainly contains carcinoma, but not in a palpable stage. The contralateral metastatic deposit may find more fertile soil, and therefore reaches a palpable stage more promptly than the metastatic deposit on the same side as the primary lesion.

No statistics are available to show the futility of operating on bilateral and contralateral metastases, nor are there any such figures known. It may again be emphasized that published statistics are the conglomerate type and include not only those cases with metastatic neck nodes but also those without metastases. These are of no value in deciding upon a procedure to be followed, and in estimating the prognosis of an individual case. The phase of the criteria dealing with bilateral metastases has been discussed in that portion of the discussion dealing with the primary growth extending to the opposite side of the oral cavity, and it need not be amplified here. There are few surgeons who now attempt eradication of bilateral cervical metastases from oral carcinoma (except lip).

7. *Distant Metastases.* It is obvious that a distant metastasis is a contraindication for neck dissection. Such metastases occur in lungs, mediastinal nodes, liver, abdominal nodes, bones and other less likely places. No known treatment can have sufficient influence on the disease in more distant regions to indicate a radical neck dissection for concomitant cervical metastases.

8. *General Condition of Patient.* Because oral carcinoma is a disease of middle life and especially of the more aged, some consideration must be given to the life expectancy of a patient when planning the treatment. It is not possible to anticipate an acute pulmonary disease, nor some of the acute cardiac disorders, but it is possible to make some estimate of the kidney function, the condition of the blood vessels, and the state of the myocardium. Diseases of the kidneys, blood vessels and heart are the causes of many of the deaths in the aged. Unless there is a fair life expectancy for the patient, no radical surgery should be undertaken. The mental shock, the physical trauma and the possible mortality should be considered in estimating the probable prognosis for each patient. This is a matter for clinical judgment and no rules can be formulated.

These criteria are based not only on the figures here analyzed, but also on the experience and statistics of a large series of cases of carcinoma of the several regions of the oral cavity. Carcinoma of the lingual lateral border are representative of the whole group, and therefore these criteria may be applied to carcinoma of the several regions (except lip).

Because no similar approach to this subject has heretofore been made, it is possible that minor changes may be necessary, but any such changes should be substantiated by statistical data on a representative

number of cases. The method of treatment must not be dictated, as in the past, by the ambitions of the surgeons, nor as at the present time, by the hopes of the radiotherapists.

It is a firm belief that if these criteria are followed, the ultimate results of the treatment of intraoral carcinoma will be improved, not only in the number of cures, but also in the better palliation of the relatively large group of the incurable patients. Surgery offers a better chance of cure in the operable group, whereas patients with advanced disease will live longer and more comfortably, with a greater chance for cure, though this chance may be slight, by radiation treatment, than by subjecting these patients in the latter group to an operative procedure which is an extreme and futile effort. Unnecessary discomfort from severe irradiation reaction, often with persistent disease, and a lessened chance of five-year survival, follows an ill-chosen irradiation program of treatment of metastatic cervical lymph nodes. Prompt recurrence of the disease, followed by severe suffering and premature death, is the result of ill-advised neck dissection.

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IRRADIATION OF CERVICAL GLANDS IN CARCINOMA OF THE MOUTH AND LIP*

By HAROLD W. JACOX, M.D.
The Western Pennsylvania Hospital
PITTSBURGH, PENNSYLVANIA

WHAT to do about the cervical lymph nodes in the treatment of cancer of the lip, tongue and mouth is still a subject about which there is sharp difference of opinion. The problem remains to be solved, even though there is a trend toward conservatism in the absence of palpable glands. This discussion is concerned with the place and technique of irradiation in the treatment and not with mortality or survival statistics.

It is generally agreed that proper surgical resection, irradiation and cautery destruction of the primary lesion in lip cancer are equally safe methods. Those who prefer one concede, nevertheless, that other methods are acceptable. There is seldom local recurrence so that the real problem is the management of cervical glands. When there are palpable lymph node metastases most workers believe adequate surgical removal together with irradiation is the procedure of choice when the glands are operable. Upon the question of whether dissection of the neck should be performed in the *absence* of palpable metastatic glands there is the greatest divergence of opinion.

The Cancer Commission of the California Medical Association a few years ago undertook to ascertain the present practice of authorities throughout the world. They found that in the presence of cancer of the lip of sufficient size, duration or microscopic evidence of deep invasion to suggest possible metastasis, two-thirds of the correspondents do not do dissection of the lymph glands if none is palpable; while one-third dissect the neck without waiting for glandular enlargement. Of the group *not* dissecting the neck in the absence of glandular enlargement about two–thirds give so-called prophylactic irradiation to the neck. If a node becomes palpable then dissection is performed. In general, the treatment of the glandular area is the same regardless of the site of the original lesion, although it is well known that cancer of the tongue and floor of the mouth metastasizes more frequently than cases primary in the lip or cheek. The majority of those who do not perform dissection of the neck when no nodes are palpable use external irradiation by either roentgen rays or radium or both.

Although irradiation has played a large part in the treatment of the glandular area, recently some have denied its value as a prophylactic measure. The definite value of this prophylactic irradiation (so named when no glands are palpable) is difficult to determine. Histologic changes in irradiated cancerous lymph nodes to be shown later indicate that the treatment is justified. Very little animal experimentation has been done on irradiated cancerous lymph nodes, probably because of technical difficulties. With nodes not palpable the assumption is that metastasis has not occurred. Why, then, irradiate the area? Because the feeling is present, but difficult of proof, that the resistance of the nodes to metastatic spread is thereby increased. On the other hand, if a non-palpable node already contains cancer it is doubtful whether external irradiation alone will destroy it completely, either by single intensive treatments or by the application of the Coutard principle of fractionated doses of high voltage roentgen rays or gamma rays. Radiologists have all seen primary lesions arrested by heavy external irradiation that has no effect upon a metastatic gland in the neck. And such heavy irradiation is usually not given prophylactically. We also see hard,

* Presented before the Pennsylvania Radiological Society, Erie, Pa., May 21, 1937.

fixed glands disappear after external irradiation, and radiosensitivity does depend on the character of the primary tumor; for example, carcinomas arising in the lymphoid tissue of the tonsils and upper throat frequently metastasize to groups of nodes rather than in a single focus, and are usually responsive to irradiation. That prophylactic irradiation is of value is suggested, of course, by certain microscopic changes and by the large percentage of workers who use it. One should hesitate to lay down any weapon that may aid in the fight against cancer. The use of insufficient dosage or anything but the strongest weapons should be discouraged. When dissection is routinely performed, less reliance is placed upon irradiation. This is perhaps as it should be, but I believe the irradiation should be given before rather than after dissection.

Are tumor cells usually destroyed in lymph glands? Histologic study of early cancerous deposits in lymph glands fails to reveal evidence of wholesale destruction of tumor cells. Many workers deny that lymph glands are the efficient "filters" they had been thought. Lymphoid tissue provides a highly fertile soil for the growth of most carcinomas.

Lymphatic dissemination from the initial lymph gland deposits is often extensive. Thus, from a carcinoma of the lip or tongue the submental or submaxillary lymph glands may become involved first, and from these the disease may extend in a series of embolic steps until every cervical lymph gland contains tumor deposits, and even the axillary and mediastinal glands may be implicated. Carcinoma in such nodes forms horny tissue, is prone to spontaneous degenerative changes, such as liquefaction, and may exhibit increased fibrotic changes after external irradiation without killing all cancer cells. On the other hand, it is possible that a few cancer cells in an early metastasis may be destroyed, whereas more of them with a better foothold will continue to grow.

I do not know exactly how much good prophylactic irradiation does. But I do know we have not controlled definite malignancy in the neck by the ordinary methods of external irradiation. I also know that when we give 1,200 to 1,800 r (measured in air) of high voltage roentgen rays to each of one or two fields within ten days to two weeks and wait six to eight weeks, we are still able to do a neck dissection with primary healing. The question of "sealing off the lymphatics" is a highly debatable one for it would undoubtedly take months for this to occur with human therapeutic doses. I do not feel that every case should have a radical neck dissection unless there are definite indications for it, since many patients do not develop palpable glands at any time. Irradiation seems more logical for prophylaxis than radical cervical gland dissection. The greatest problem in the management of these nodes is the consideration of indications and contraindications for a radical or partial cervical dissection and of when to employ radiation therapy instead of surgery. The best answer to this problem has been furnished by Dr. James J. Duffy of Memorial Hospital, New York (quoted by Pack[2]).

Indications	Contraindications
1. Metastases limited to one node or group of nodes	1. No apparent metastatic involvement of nodes
2. No perforation of capsule of lymph nodes	2. Perforation of capsule by carcinoma
3. Primary lesion controlled or controllable	3. Primary lesion uncontrolled or uncontrollable
4. Opposite side of neck free from disease	4. Crossed metastasis or bilateral metastasis present
5. Primary lesion limited to one side of oral cavity	5. Extension of primary lesion to or beyond the midline
6. Primary lesion composed of highly differentiated cells	6. Primary lesion composed of undifferentiated cells
7. No distant metastases	7. Distant metastases present
8. Patient in good health	8. Patient in poor general health or aged
All these indications should be present for dissection.	Any one of these contraindications preclude dissection.

Thus the operability of the cervical nodes is determined by the grade of malignancy of the primary lesion as well as by the extent of the metastases.

The technical procedures I prefer are:

1. In the absence of visible or palpable nodes, the lymph drainage areas are irradiated with high voltage roentgen rays to each side of the neck from the mandible to

the clavicles, protecting the parotid glands. Usually from 1,200 to 1,800 roentgens per field is given within ten days to two weeks; 200 r is given per day until there is a definite biological reaction on the skin or mucous membranes. This has not interferred with a later neck dissection if nodes develop. The need for regular follow-up examinations is emphasized.

2. When the patient has isolated movable nodes in the neck, either one or both sides are treated as above with roentgen radiation first. Radical dissection follows in from two to six weeks if the primary lesion is controlled and the nodes are still palpable. Further irradiation is not given unless there is definite recurrence.

3. If the nodes are fixed, external irradiation is given to both sides of the neck and, after the reaction has subsided in from two to four weeks after the series, a wide surgical exposure allows the accurate implantation of radium needles. These are usually placed in a radial fashion if the mass is large enough or parallel to the long axis of a smaller node. From two to six or even eight 10 milligram needles with a wall thickness of 0.5 mm. platinum are left in place from eighteen to thirty hours. Usually the process is extensive enough so that the needles are not too large, and radon seeds are seldom used. I have seen the disease arrested with this combined technique, but the result is usually only palliative.

4. If the glands have perforated the skin in far advanced cases with crater formation and secondary infection, caustic irradiation of 5,000 to 7,000 r applied to the rim of the crater after a full high voltage series will occasionally produce healing. If the area is greater than 5 cm. in diameter the above method is not applicable.

The practice of removing as much of the neoplastic glands as possible and implanting radium is one which has many advocates. I have always felt that the danger of dissemination by emboli from this procedure is greater than the good obtained. I believe irradiation before the radium application will cause the growth to shrink with less danger of spread and that needle puncture also will be less harmful.

The following cases illustrate some of the points just mentioned:

Case 1. J. C., male, laborer, aged seventy, was referred to the Western Pennsylvania Hospital in August, 1935, with a tumor about 2×2×1 cm. in size to the left of the midline of the lower lip. The onset was five years before with a crack in the lip which would heal intermittently, but for the past five weeks a tumor had been growing rapidly. No nodes were palpable.

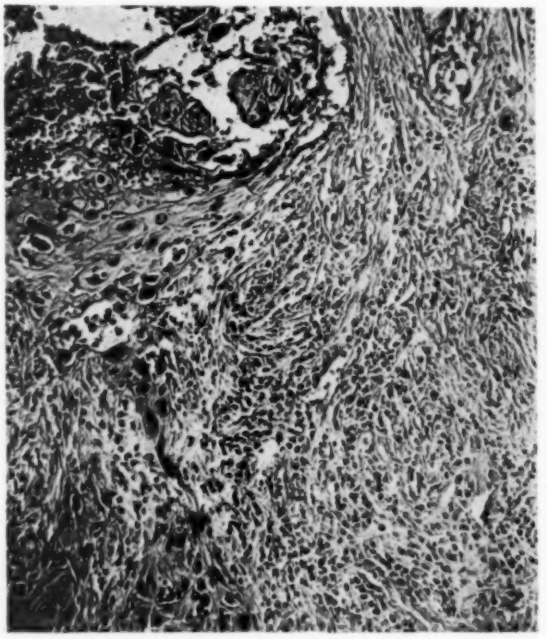

Fig. 1. Case 1. Photomicrograph of cervical lymph node after intensive irradiation. Necrosis is seen in the upper left corner, while extensive fibrosis with associated monocytic infiltration is present throughout the greater portion. The small masses of tumor cells are seen along the left side and bottom. These cells are sparsely distributed throughout the specimen.

Electrosurgical removal and microscopic study of the lesion showed it to be a well differentiated squamous cell carcinoma, and 1,235 r of medium wave length roentgen rays was given locally in one sitting. No irradiation was given over the cervical glands.

Healing promptly occurred and the patient remained well for eight months. When I first saw him in June, 1936, he presented a hard, painless, movable mass about 3.5×3×2 cm.

under the left lower jaw of four weeks' duration. He received 2,400 r of high voltage roentgen rays (200 kv., 0.5 mm. Cu filtration) to the the left side of the neck including the lower jaw with a portal 12×15 cm. in size within a period of two weeks, giving 200 r per day. The irradiation produced approximately 50 per cent reduction in size. There was no radiation sickness. Two weeks following the last treatment a left radical neck gland dissection was done, the microscopic report being, "metastatic squamous cell carcinoma, well differentiated with marked degeneration, necrosis and fibrosis" (Fig. 1).

There was a brilliant erythema with moderate desquamation of the skin over the portal, but the wound healed normally, and when the patient was last heard from, April 14, 1937, there was no evidence of recurrence or metastases and he was in perfect health.

Case 11. Mrs. E. J., a widow, aged eighty-eight, was first seen in the Tumor Clinic of the Western Pennsylvania Hospital on January 15, 1937, complaining of a sore tongue and a lump in the left cervical region. The history was indefinite, but the condition was thought to have been present for eighteen months. Upon examination a diffusely indurated, ulcerated lesion 3×2.5×2 cm. was situated on the left posterolateral border of the tongue and floor of the mouth. In the left cervical region a hard fixed lymph node about 4×2×2 cm. was found. The condition of the mouth was unhygienic. A biopsy from the tongue showed an adult type of squamous cell carcinoma with pearl formation.

A series of high voltage roentgen treatments (200 kv., 2 mm. Cu) to the left jaw and neck through a portal 12×15 cm. was started, applying 100 r daily. After twelve days, ten radon seeds, a little less than 1 millicurie each, with a wall thickness of 0.3 mm. gold, were implanted in the tongue and floor of the mouth to remain permanently. The total dosage was 133 mc-hr. per cubic centimeter of tissue and 1,200 r of external irradiation given in fifteen days. This external irradiation produced mild radiation sickness which required no treatment, a dull erythema of the skin and a typical mucositis of the buccal and pharyngeal membranes with hoarseness and difficulty in swallowing. The intensity of the reaction in both the normal and pathologic tissues was much greater than might have been expected from the amount of external irradiation given. The reaction lasted about ten days and was treated by equal parts of honey and glycerine and powdered aspirin insufflation. There followed an approximately 50 per cent reduction in size of the gland.

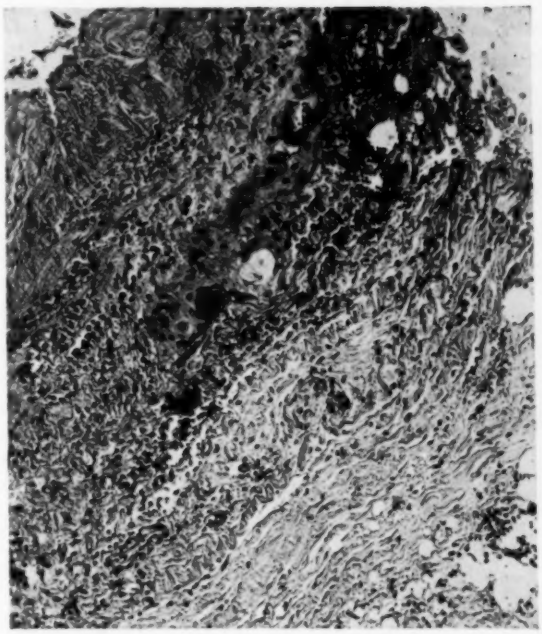

Fig. 2. Case 11. Photomicrograph of effects similar to Figure 1. There are even fewer carcinoma cells found. The necrosis is not represented in this illustration.

Five weeks following the completion of the roentgen therapy, the gland was exposed surgically and two 10 mg. platinum needles with a wall thickness of 0.5 mm. were inserted in its periphery parallel to each other and the longitudinal axis. At the same time a biopsy of the gland was done which microscopically showed a few well differentiated squamous carcinoma cells with much degeneration, necrosis and fibrosis (Fig. 2). Grossly, the tissue was thoroughly broken down with caseation necrosis, but no evidence of lymphoid tissue, infection or neoplasm was found.

When last seen May 6, 1937, the patient had gradually recovered, was in fair condition and there was satisfactory retardation of the neoplasm.*

SUMMARY

1. The real problem in carcinoma of the lip and mouth is the treatment of the cervical glands.

2. High voltage roentgen radiation to the lymph-bearing areas and lymph nodes is

* This patient died in the summer of a cardiac attack.

valuable as a prophylactic measure in all cases.

3. Prophylactic irradiation properly given will not damage the tissues enough to contraindicate intensive irradiation if needed in the future.

4. When isolated inoperable nodes are present, roentgen irradiation supplemented by interstitial radium is the method of choice.

5. Roentgen irradiation for palliative purposes is advisable in the advanced group.

6. Histologic changes in cervical glands treated by external irradiation indicate the value of this procedure.

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IS ROENTGEN IRRADIATION OF VALUE IN THE TREATMENT OF PULMONARY METASTASIS FROM MAMMARY CANCER?*

By NORMAN TREVES, A.M., M.D., F.A.C.S.
Associate Attending Surgeon, Memorial Hospital
NEW YORK CITY

COMMENTING, in 1924, upon the roentgen treatment of pulmonary metastasis from inoperable breast cancer, Lee and Herendeen stated:

> This difficult problem is far from solution at the present time, for one is rather reluctant to attempt vigorous treatment of pulmonary metastasis. Though a slight regression might be obtained, there is always the possibility at the same time of seriously impairing the patient's nutrition and general resistance against the disease. Further, the treatment of the breast and drainage areas introduces a very considerable amount of radiation into the deeper tissues of the chest with at least some favorable effect upon the metastasis there. Nevertheless, we are continually making an effort to more adequately treat metastasis in the lung by changes in technic. A few selected cases with metastasis to the lungs have been treated by high voltage without very satisfactory results to date.

In the thirteen years since this statement appeared there has been a great improvement in roentgen equipment and technique. In spite of this, Leddy and Desjardins in 1936 epitomized their results in treating metastatic mammary carcinoma of the lung.

> Metastasis to the lungs or pleura is a most unfortunate development. With carefully given roentgen treatment, we have been able, in some cases in which the patients have been in good physical condition, to lessen dyspnea from enlarged hilar nodes or to decrease the frequency of aspiration for effusion into the pleural space. We have little evidence of the beneficial effect of radiotherapy on parenchymal metastasis, except as a rare incident.

In the intervening years there have appeared reports on an isolated instance of pulmonary metastasis that has responded in a marked degree to roentgen irradiation. While these reports are interesting (and should be published) they tend to impress the clinician with the fact that all cases of metastatic lung cancer, if adequately treated, should respond in a like fashion.

For this reason, Gantenberg, in 1933, reported the improvement following high voltage roentgen therapy of a case of metastatic mammary carcinoma to the lung. The treatment consisted of nine series of radiation exposures for a total of 745 per cent H.E.D. The total duration of life, however, was less than two years following operation. Borak, in 1933, reported improvement in 2 cases of secondary involvement of the lung from breast cancer. But Grosche gave so little information in his Freiberg thesis in 1932 that one is unable to evaluate the results of treatment. De Luca, in 1936, reported satisfactory regression of a single case of pulmonary metastasis of the sarcomatous type. d'Halluin and Belle believe that some relief may be obtained and life prolonged by treating pulmonary metastasis with high voltage roentgen rays.

On the other hand, Ackland considers it impossible to benefit the patients who have visceral metastasis. With this opinion Leddy and Desjardins are in accord.

In a series of 363 patients with recurrent inoperable carcinoma of the breast, reported in 1925 with the late Dr. Burton J. Lee, we found that 10 per cent came to the clinic with pulmonary metastasis (the fourth most frequent site). Since many of the recurrent cases, as well as the primary cases, develop this fatal type of metastasis we were hopeful that deep therapy would

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

alleviate the symptoms and prolong life. For this reason we treated a group of patients with metastatic breast cancer of the lung. There were 59 cases in this group, which were studied to form the basis of this report. The cases were first observed during the three years from 1931 to 1934. These 59 cases comprised a group of 38 patients with pulmonary metastasis treated by roentgen irradiation and a group of 21 cases with pulmonary metastasis untreated, which were used for comparison. The 38 cases which were treated constituted consecutive patients observed in the breast clinic between 1931 and 1934, whose general physical condition we felt could stand the additional radiation therapy for the pulmonary metastasis. While it is obvious that more untreated cases might have been used for comparison, we believe the cases analyzed represented a fair cross section of the untreated cases. In the treated group the left breast was involved in 21 instances, the right in 16 and both breasts were involved in 1 instance. There were 2 cases of carcinoma in the male breast in the series of treated patients. In this group 12 were classified as primary operable, 12 primary inoperable and 14 recurrent inoperable.

SYMPTOMS AND CLINICAL SIGNS OF PULMONARY METASTASIS

The most frequent early symptom of pulmonary metastasis to lungs or pleura is cough. Indefinite pain in the chest and a sense of oppression and shortness of breath are the next most frequent complaints.

Earlier Signs. According to Craver, the earliest physical sign in detecting pulmonary metastasis is a "peculiar limitation of breath sounds, especially marked during inspiration, covering a limited area of the chest." This finding may be accompanied by fine crackling râles during inspiration. There may be no change in tactile fremitus, percussion note or alteration in the vesicular quality of the breath sounds. Dyspnea and cyanosis may appear early but usually develop later in the course of the disease. The signs of metastases are more frequently discovered in the lower half of the chest posteriorly.

Later Signs. As the metastatic deposits increase in size, the signs become accentuated and more diffuse, the change affecting a large part of one or both lungs. The percussion note is impaired and the crackling râles on auscultation are replaced by sibilant or sonorous ones, increasing in number and loudness. Expansion of the chest may be limited visibly, due either to the pleural effusion which may develop or to extensive parenchymatous infiltration. Cough, often intractable, develops. It may be productive, but frequently produces little or no sputum. Bloody expectoration rarely occurs. Dyspnea increases and cyanosis may be marked.

We have analyzed the group of 59 cases and find that the most frequent, solitary symptom of pulmonary metastasis was cough, which occurred in 41 instances. Shortness of breath was the next most frequent, occurring in 34 cases. Pain was present in 16 patients, effusion in 12 and bloody expectoration in 7. It should be noted that bloody expectoration, which so often accompanies primary lung cancer, was an infrequent symptom of this complication of mammary carcinoma. However, there were 11 patients in whom no signs or symptoms occurred, the diagnosis of pulmonary metastasis being made upon the findings of the chest film alone.

DIFFICULTIES IN MAKING A POSITIVE ROENTGENOGRAPHIC DIAGNOSIS OF PULMONARY METASTASIS

The findings in many of the films reviewed in this series were suggestive of early pulmonary metastasis but a positive diagnosis could not be made. It was only by a close check-up of the cases with repeated chest films that Herendeen was able to state that there was definite evidence of pulmonary metastasis. In several cases, in which a diagnosis of pulmonary metastasis was made, the patients lived for periods of ten years or more and these cases were ex-

cluded from this study, as it was obvious that the roentgen findings were in error. It should be stated that certain inflammatory lesions in the lung (unresolved pneumonia and pleurisy), chronic tuberculosis, heart disease and radiation pleuropulmonitis may cause confusing roentgen findings, and especially when these findings are associated with mammary cancer a questionable diagnosis may be made because of its existence.

Figure 1 is a case of carcinoma of the breast, treated by roentgen irradiation and surgery, in which metastasis and radiation pleuropulmonitis occurred. With this is an associated diaphragmatic hernia. This roentgenogram is shown to illustrate a difficulty encountered in roentgen diagnosis.

ANALYSIS OF THE GROUP

The group of cases with pulmonary metastasis from breast cancer were divided into three clinical groups and into three groups according to the pathological diagnosis roentgenographically. There were 12 patients in the primary operable group with pulmonary metastases, 12 in the primary inoperable group and 14 in the recurrent inoperable group. The average age of the treated group (38 cases) was 50.5 years. The average age of the untreated group (21 cases) was 50.2 years. The average interval between the appearance of symptoms and the development of pulmonary metastasis in the treated group was 22.1 months, while in the untreated group it was 11.1 months. Therefore the cases which were treated showed a greater interval of time between the appearance of symptoms and the development of pulmonary metastasis than the untreated group in a ratio of about two to one. This difference may affect the survival period, but the entire duration of disease from the appearance of the first symptom to death in the treated group was 16.7 months, while the survival period of the untreated group was twenty-six months.

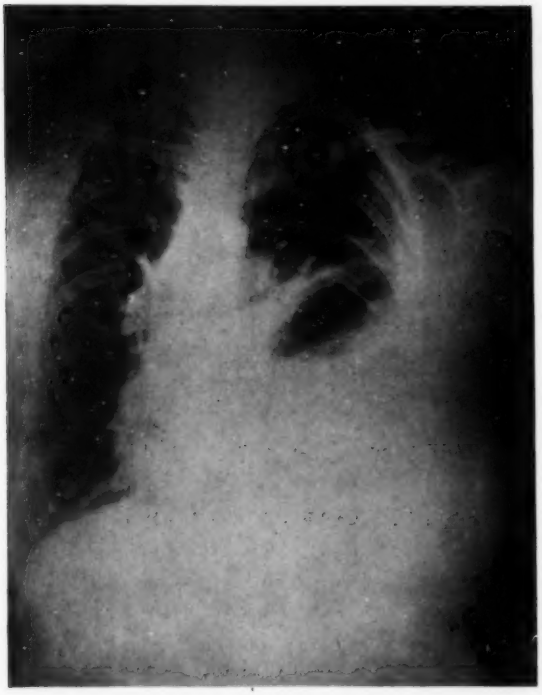

Fig. 1. Metastasis to the right hilum. Radiation pleuropulmonitis, left side. Diaphragmatic hernia, left side, with cardiac portion of stomach in left pleural cavity.

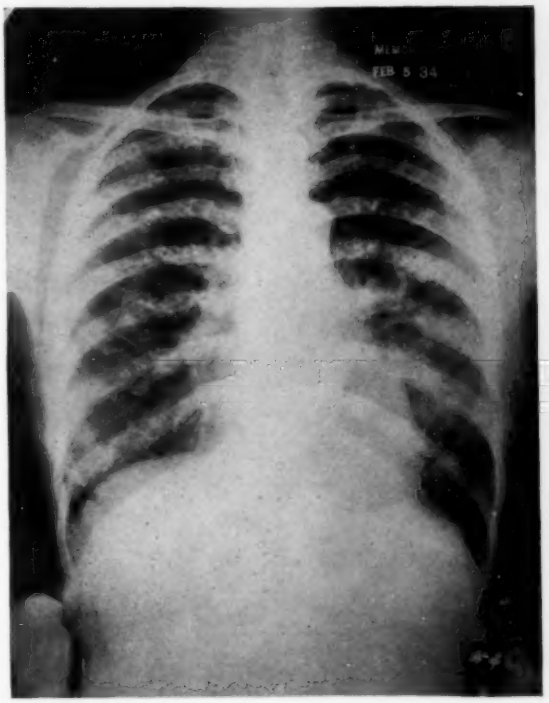

Fig. 2. Diffuse infiltrating metastases to the pleura from cancer of the breast. Note the hazy streaking of the lymphatics.

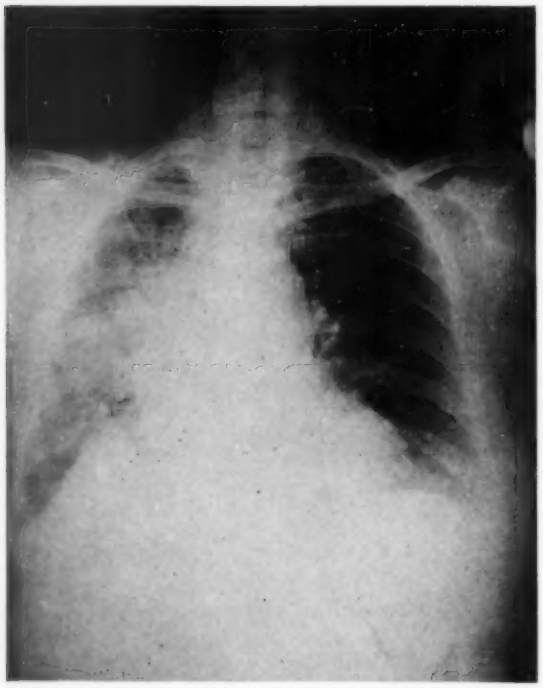

FIG. 3. Metastatic involvement of the lymph nodes at the right hilum with extension into the lymphatics at the root of the lung.

We have proposed a classification of the pathological groups under the three following headings: (1) the diffuse or infiltrating group, composed of those cases in which the spread of the disease was located in the pleura, or diffusely through the lymphatics (Fig. 2); (2) the hilar group, where the first appearance of metastasis was confined to the hilar nodes (Fig. 3). In this instance, secondary extension may occur by way of the lymphatics, but the cases were considered of hilar origin if only the mediastinal nodes were the first site of involvement; (3) the third group, and the most infrequent one, was the nodular or sarcomatous type of metastases (Fig. 4).

TECHNIQUE OF ROENTGEN THERAPY

These patients were treated with high voltage roentgen rays using 200 kv., 0.5 mm. copper filtration and for the most part 70 cm. skin-target distance. The size of the skin portal was usually 200 sq. cm. The patients were usually treated through four portals anterior and four portals posterior. The total dose per portal for the eight fields has been used to group the results of treatment.

The cases were grouped according to the total number of roentgens given per portal. Those that received 1,000 r (a total of 3 threshold erythema doses at a point 10 cm. below the skin surface at the hilum), those cases which received a total of 1,500 r per portal (4.5.T.E.D.) and those cases which received up to a total of 2,000 r (6 T.E.D.). These calculations for the threshold erythema dose at a depth of 10 cm. below the skin have been made by Edith H. Quimby of our Physics Laboratory with the radiation factors above noted. Twenty-three patients were treated through eight portals with a total dose per portal up to 1,000 r (3 T.E.D.), 16 patients with a total dose per portal up to 1,500 r (4.5.T.E.D.) and 2 with doses up to 2,000 r per portal (6 T.E.D.) (Table 1).

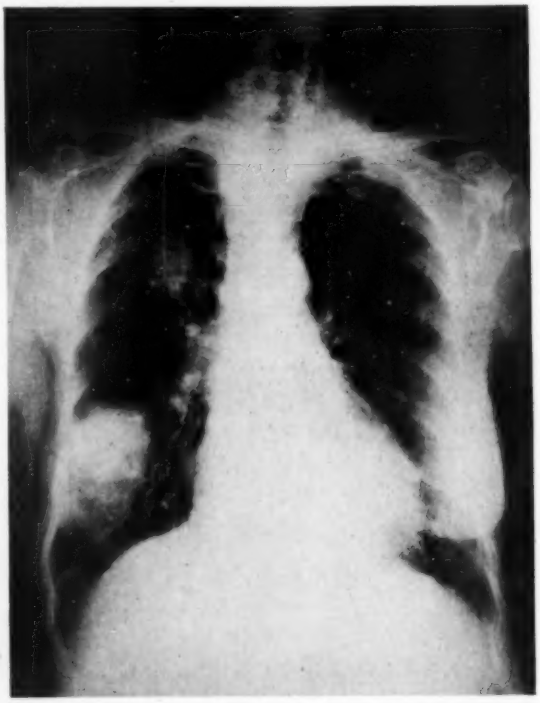

FIG. 4. Discrete nodular metastasis to the lung parenchyma (sarcomatous type).

ANALYSIS OF TREATMENT

For the purpose of analysis, however, we have felt that grouping the patients according to the roentgenographic pathological types was the fair way of determining the results of treatment. There were 15 patients with diffuse pulmonary metastasis, 10 treated with 1,000 r per portal, 3 with 1,500 r and 2 with 2,000 r. The average survival period after the treatment was 10.9 months. Comparing this with 14 untreated cases of the diffuse type, the average survival period was 29.8 months. In the group with metastasis to the hilar nodes there was a total of 16 cases, 11 treated with 1,000 r per portal and 5 treated with a total of 1,500 r per portal. The average survival period after the beginning of treatment was

TABLE I

ANALYSIS OF RADIATION TREATMENT

Clinical Group	Total Cases	Total r per Portal					
		800–1,000		1,200–1,500		2,000	
		Approximate tissue dose at center of lung—T.E.D.*					
		3		4.5		6	
Primary Operable		Cases	Av. Duration	Cases	Av. Duration	Cases	Av. Duration
Diffuse	5	3	12 mo.	2	5 mo.		
Hilar	4	3	15	1	9		
Nodular	3			3	7		
	12	6	8.8	6	6.6		
Primary Inoperable							
Diffuse	6	3	26	1	4	2	11
Hilar	4	3	16	1	6		
Nodular	2	2	6				
	12	8	16.7	2	5	2	11
Recurrent Inoperable							
Diffuse	4	4	14				
Hilar	8	5	31.5	3	15		
Nodular	2			2	13.5		
	14	9	22.7	5	14.4		
Total	38	23	16+	13	8.6	2	11

* T.E.D. = Threshold erythema dose. This is the total dose from all portals, as calculated by Edith H. Quimby, Associate Physicist, Memorial Hospital.

15.4 months, compared with 5 patients in the untreated group, who lived for forty months. There were only 7 patients with the sarcomatous or nodular type of metastasis. Two were treated with 1,000 r per portal and 5 with 1,500 r per portal. These lived an average of 8.1 months while the 2 patients with the nodular type of pulmonary metastasis from mammary cancer in the untreated group lived for thirty-nine months. The average duration of life in the 38 patients with pulmonary metastasis, treated with high voltage roentgen rays, was 11.4 months, while the average survival period of untreated mammary cancer in the lung for 21 patients was 35.9 months. It is apparent from these figures that the patients with untreated pulmonary metastasis live more than three times as long as the treated group. There may possibly be factors influencing these figures which we have not taken into consideration, but it should be pointed out that the average age of the two groups was the same and that the total survival period of the treated group was 16.7 months while the total survival period of the untreated group was twenty-six months. A factor which has not been taken into consideration in reporting these cases is an analysis of the pathological types represented in this group. A future study including the types of breast cancer, the pathological grading and the node involvement may possibly affect the end-result figures (see Table II).

TABLE II

RESULTS OF TREATMENT IN ROENTGENOGRAPHIC GROUP. AVERAGE DURATION OF LIFE IN TREATED AND UNTREATED CASES

Group	Roentgen Treatment Per Portal	Average Duration—Months			
		No. cases	Treated	No. cases	Untreated
Diffuse	Up to 1,000 r	10	17.3 mo.		
	1,500	3	4.5		
	2,000	2	11.0		
		15	10.9	14	28.9
Hilar	Up to 1,000 r	11	20.8		
	1,500	5	10.0		
	2,000	0			
		16	15.4	5	40.0
Nodular	Up to 1,000 r	2	6.0		
	1,500	5	10.2		
	2,000	0			
		7	8.1	2	39.0
Average		38	11.4	21	35.9

In only one of the cases was there definite evidence of marked clinical improvement following roentgen treatment of the metastatic pulmonary condition. This was a patient in whom the metastasis was of the nodular type and although there was marked clinical improvement, the roentgenogram of the chest eight months after completion of treatment showed marked extension of the disease (Figs. 5 and 6). Of the 38 patients who received high voltage roentgen treatment, 5 showed slight improvement while the rest were completely

refractory to treatment as far as amelioration of symptoms was concerned. In no instance was the rate of accumulation of effusion affected. In the untreated group of 21 patients, 2 lived for seventy-five months after a positive chest film was obtained. These represent the longest duration in the untreated group. However, the shortest duration was three months. With the information which we have at hand, we are unable to explain the wide variation in the duration of the disease. We are unable to explain why 2 patients with visceral metastasis present should live for such long periods of time. In the treated group, the longest length of life noted after the institution of treatment of pulmonary metastasis was sixty-six months and the shortest two months. Again there is a marked variation in the survival periods.

DISCUSSION

In considering the results of treatment, one immediately wonders how these patients would have reacted to larger doses of roentgen radiation. One must always bear in mind that a patient with metastatic cancer and especially breast cancer metastatic to the lung is not in too good physical condition. Consequently, we have felt that these patients were not able physically to withstand more radiation than this group received. Most of these patients are anemic and any cycle of high voltage roentgen rays given to eight portals over the chest must necessarily irradiate intensively the entire blood volume of the body. One must therefore keep in mind that while possible growth restraint may be brought about by irradiating pulmonary metastasis from breast cancer there is always the danger of producing a severe secondary anemia. Besides, other changes may occur in the lung following intensive roentgen irradiation, which together with the anemia produced by intensive radiation therapy, may be as formidable as the disease itself.

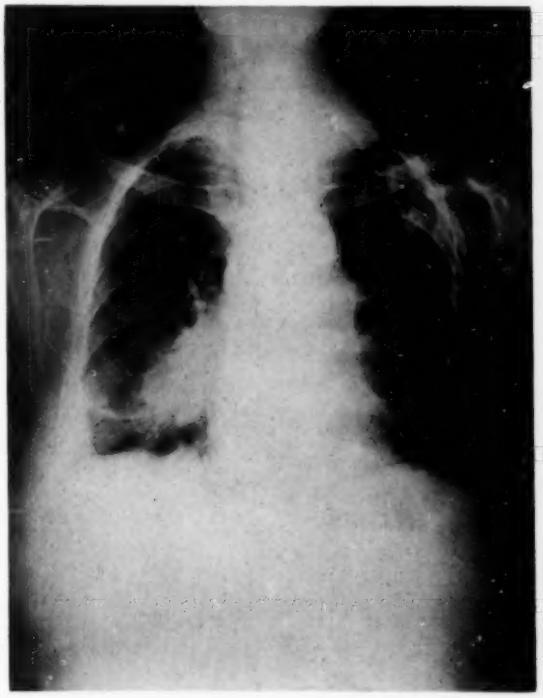

Fig. 6. Roentgenogram of the same case as Figure 5 after high voltage roentgen therapy. Film taken eight months after the preceding one. There was marked clinical improvement in this patient. There is, however, marked extension of the disease.

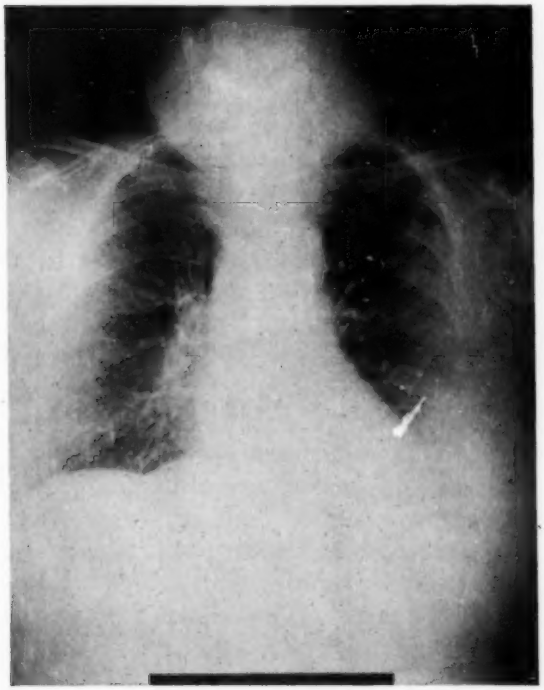

Fig. 5. Metastasis to the root of the right lung with enlargement of the hilar lymph nodes.

FIG. 7. Radiation pleuropulmonitis of the segmental type.

In 1926, Desjardins called attention to the reaction of the lungs and pleura to high voltage roentgen rays. While Groover, Christie and Merritt and Evans and Leucutia had before reported on the intrathoracic changes induced by heavy irradiation, it was Desjardins who gave the name to this condition, which has now been generally accepted, namely "pleuropulmonitis."

McIntosh reported a small series of cases of pleuropulmonitis and was of the opinion that this effect was a quantitative and not a qualitative one. She found that anywhere from 2½ to 6 T.E.D. in the hilum of the lung may produce this condition. Another possible influence is the age of the patient and arteriosclerosis of the lungs and pleura. The symptoms of radiation pleuropulmonitis are usually distressing and severe. While radiation pleuropulmonitis very often clears up and the symptoms disappear, when its symptoms are added to those of pulmonary metastasis the patients experience even greater subjective and objective discomfort. Adding intensive radiation therapy for the pulmonary metastasis and thereby producing this added pulmonary pathology makes the patient more uncomfortable than allowing the metastasis to go untreated.

Roentgenographically, there are two types of radiation fibrosis, the diffuse and the segmental. The latter form is much more common (Fig. 7). These patients evidence increased and constant cough, dyspnea, pain and cyanosis.

Adair recently called attention to this complication in the preoperative roentgen treatment of primary operable carcinoma. He does not venture an opinion as to the etiology except to state that large doses of deep roentgen radiation may produce it. It was found to have occurred at all ages, but a preëxisting bronchitis was not believed to be a contributing cause. Adair found that it occurred more frequently in the younger patients and concluded that this was because heavier irradiation had been given to these cases.

We have recently examined the histories of 30 cases of primary operable carcinoma receiving a preoperative roentgen cycle consisting of exposure through five portals with a total of 1,800 r per portal. Twenty-four cases, or 80 per cent, developed radiation pleuropulmonitis. Since there were 13 cases in the treated group which received up to 1,500 r (4.5 T.E.D.) per portal at the hilum, one may well consider that with the methods at hand effective irradiation without serious complications cannot be delivered.

SUMMARY

(1) Thirty-eight cases of pulmonary metastasis from mammary cancer have been studied to ascertain the clinical and roentgenographic effects of therapy. The dosage has been from 800 r to 2,000 r per portal.

(2) The roentgen manifestations of metastatic mammary carcinoma have been indicated. Three distinct types occur: the diffuse, the hilar and the nodular.

(3) The treated group of 38 cases has

been compared with an untreated group of 21 cases. The average duration of life from the beginning of treatment of the pulmonary metastasis to death was 11.4 months in the former group. The untreated cases lived for 35.9 months. Although the treated and untreated groups were comparatively small, one must conclude from these figures that patients with pulmonary metastasis from mammary cancer live longer if untreated.

(4) Radiation pleuropulmonitis was a severe complication in the preoperative treatment of mammary cancer. It may be a complication in the treatment of the pulmonary metastasis.

CONCLUSIONS

Patients with metastasis to the lung from a primary mammary cancer are usually in poor general condition; in addition, they may be anemic. Any effect from radiation therapy in bringing about growth restraint would increase the anemia. Radiation pleuropulmonitis, a complicating factor in preoperative radiation therapy of the breast, would be superimposed on the secondary disease, increasing the distressing pulmonic symptoms. The treatment of pulmonary metastasis has resulted in few instances of marked symptomatic relief. Furthermore, the patients lived for much shorter periods of time.

While the group studied in this report is a comparatively small one, it represents a much larger series of cases of pulmonary metastasis treated by roentgen irradiation than any other reports on this subject which we have been able to find in the literature. It is possible that a larger series of treated cases with a larger control group may produce a statistical result at variance with our figures.

Unless newer methods for irradiating the lung for metastatic disease are developed which are more effective than those considered in this report, we must conclude that roentgen therapy, with rare exceptions, is of doubtful value in controlling mammary cancer which has invaded lung.

Acknowledgment is made to Dr. James J. Duffy for his helpful cooperation in initiating this study and for valuable suggestions in analyzing the results of treatment.

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PROTRACTED ROENTGEN THERAPY OF PHARYNGEAL LYMPHOSARCOMA

By ALBERT JUTRAS, M.D.
MONTREAL, CANADA

FROM 1919 to 1928 inclusive, 64 cases have been classified and treated at the Institut du Radium de l'Université de Paris, as lymphoid sarcoma of the pharynx.

Under the heading *lymphoid sarcoma* or *lymphosarcoma*, we are to consider all those various malignant neoplasms arising from lymphatic tissue and characterized histologically by a proliferation of more or less typical cells of lymphoid origin and of which the normal lymphocyte is the mature expression.

No effort was made to subdivide this group according to more or less recent nomenclatures, since the minute histological differences described by modern pathologists are not yet sufficiently well defined, and especially since the extreme radiosensitivity of nearly all lymphatic tumors renders microscopic distinctions of no practical value to the roentgenologist.

In spite of the extraordinary sensitivity of lymphosarcoma, it is astonishing how few cures of long duration of such tumors can be found among statistics. Of course, even in the early days of radiotherapy, isolated good results were published; but, as a rule, claims seemed to be premature and the lack of details has led to no convincing conclusions.

This has been true in regard to lymphosarcoma originating from the pharynx, although Gunsett, Quick, Holthusen, Harmer, and others, have reported success in many instances. Berven, Forssell's coworker in the Radiumhemmet, Stockholm, presented in 1931 a most interesting paper on the subject. Twelve of his 35 patients treated by irradiation for lymphosarcoma of the tonsils were still living after a follow-up of five years or more. These figures mean 34.3 per cent of cures, a percentage which is quite comparable to the results obtained by roentgen therapy at the Institut du Radium de Paris.

Furthermore, we wish to emphasize that, although it may be of aid in evaluating cancer cures, the five-year period is no absolute criterion, especially when dealing with lymphosarcoma. We have before us a case in which a metastatic recurrence appeared after being in abeyance for six years. Therefore, the use of the word *cure* in this paper only signifies the absence of actual symptoms arising from the tumor growth.

MATERIAL

In the present work, covering the 1919–1928 period, are reported the 48 cases treated by roentgen rays alone, which gave 16 five-year cures (34.8 per cent). From the total of 64 patients admitted for pharyngeal lymphosarcoma during that time, we are thus eliminating 18 cases which received radium treatment either with or without roentgen therapy. All the patients treated with radium died more or less rapidly. They do not permit any fair comparison since treatments were given with obsolete techniques, in the experimental phase of radium and before telecurie therapy was developed.

Sex Incidence. Of the 46 patients in the present study, 25 were male and 21 were female. In each group 8 patients remained cured over five years, giving respectively 32 and 38 per cent permanent results.

The figures in Table 1 stress two points: first, that lymphosarcoma, although more frequent in adolescence than epithelioma, makes no important exception to what is known as cancer age, 38 of 46 patients (83 per cent) being over forty; secondly, that the best end-results are observed between the ages of forty and sixty.

Children and young adults have shown in this special form of neoplasia a more rapid evolution and less response to treatment.

General Results. As previously men-

Table I

AGE INCIDENCE

Number of Cases Treated	Age	Number of Cases Cured
2	11 to 20	1
2	20 to 30	0
4	30 to 40	2
12	40 to 50	5
12	50 to 60	5
10	60 to 70	2
4	70 to 75	1

tioned, 16 out of the 46 patients (34.8 per cent) survived over five years; 5 patients submitted to roentgen therapy before 1923 have died. Of the remaining 41, sixteen were considered as cured in 1934, that is, 39 per cent of the cases of the 1923–1928 period. They are classified as follows:

Table II

Number of Cases Treated	Date of Treatment	Number of Cases Cured	Actual Duration of Cure
3	1923	2	11 yr.
6	1924	1	10 yr.
8	1925	3	9 yr.
7	1926	2	8 yr.
13	1927	6	7 yr.
4	1928	2	6 yr.

Local Cures. In 6 patients who came for treatment when the condition was too far advanced, it was not possible to determine in what part of the pharynx the sarcoma originated.

In the other 40 cases, the point of origin was attributed as follows: 24 from the palatine tonsils, 13 from the tonsils of the cavum (pharyngeal and paratubular), 3 from the lymphatic tissue at the base of the tongue.

In 37 cases no sign of regional recurrence was registered, which means 80 per cent of perfect and controlled local healing.

The unsuccessful results can be classified as follows: 1 patient was lost sight of; 1 patient succumbed to a hematemesis shortly after the treatment; 2 patients suffered from pharyngeal recurrence shortly after treatment; 3 patients suffered with an invasion of the cavity of the orbit and endocranium progressing from a pharyngeal lesion, most likely not well sterilized or due to local recurrence; 2 patients were not cured locally because the irradiation could not be conveniently carried out.

Notwithstanding odd exceptions, the local cure has been relatively constant. On that account we may definitely state that we find, as regards radiocurability, no difference between lymphosarcoma arising either from the cavum, from the tonsils or from the posterior part of the tongue. Our impression is that the obstacle to irradiation by the surrounding bony tissues of the cavum is compensated for by an earlier diagnosis as a result of earlier functional disturbances and by slighter invasion of the cervical lymphatic ganglia.

Size of Primary Tumor. These same remarks apply to the size of the primary tumor. The frequency of local cures would make the extension of pharyngeal lymphosarcoma of secondary importance were it not for the fact that large involvement would increase the chances of metastasis. In other words, large and small lesions in the pharynx would give nearly equal good late response to roentgen irradiation, not considering the widespread lymphatic dissemination more common with the larger lymphosarcomata. By this, we do not maintain an absolute parallelism between the size of the primary growth and the adenopathy, since in certain subjects in whom the pharyngeal tumor is voluminous, there is little or no adenopathy, whereas in some less extensive lesions the glandular reaction is more pronounced.

Adenopathy. The condition of the lymphatic system is the most important single factor in the prognosis of lymphosarcoma, though the invaded lymph glands are also extremely radiosensitive.

Of 10 patients who revealed no adenopathy, 7 remained cured for five years and more (70 per cent); 8 survived four years. Among the 30 patients in whom the

adenopathy was limited to the cervical lymph nodes, 9 (19.5 per cent) are still living. In the 6 remaining cases in which coexisted, with the cervical adenopathy, enlarged lymph nodes in other areas, the results have been poor in all.

RECURRENCES AND REPEATED TREATMENTS

In the series of 46 patients treated by roentgen therapy alone, it has been necessary to treat a certain number of pharyngeal recurrences, cervico-glandular and even distant metastases. These treatments have given only palliative results except in 1 patient who has survived for five years with a pulmonary mediastinal metastasis. In short, of those 36 patients who received only one series of roentgen treatments, we have noted 15 survivals of more than five years (41.6 per cent); of 10 patients having received repeated irradiations, there has been only 1 successful case (10 per cent).

PRINCIPLES OF PROTRACTED ROENTGEN THERAPY IN LYMPHOSARCOMA

The fact that the cures were few in contrast to the rapidity with which lymphoid tumors disappeared, locally, under the action of roentgen rays, was ascertained from the early experiments. Many authors then maintained that roentgen rays only destroyed the irradiated parts of the tumor but in no way retarded the fatal outcome.

Early methods of irradiation having led to constantly fatal results, Coutard directed his attention to newer techniques in the use of roentgen therapy. This he brought to a degree of accuracy about 1923.

To duplicate Regaud's experimental works and to blaze a trail in this new direction, Coutard tried to apply to roentgen therapy of lymphosarcoma of the pharynx the same principles which he had already used in the treatment of carcinoma of the same region.

Regaud had noted a difference in the radiosensitivity of primary basal cells of normal and carcinomatous tissues; Coutard, therefore, was brought to believe that these differences also existed in lymphosarcoma cells, some being more resistant and surviving destruction by irradiation would bring about recurrences or even retarded metastases.

The results obtained by this change in irradiation methods were most encouraging from the start, as may be seen by referring to Table 1.

Let us now discuss those technical methods by which roentgen therapy has continually made progress.

QUALITY OF RADIATION

The techniques of irradiation were modified in relation to better apparatus, such as generators and tubes.

Transformers with open magnetic circuit were replaced by transformers of closed magnetic circuit with mechanical rotating rectifiers, and later, by generators known as "constant potential machines," so that the voltage on the secondary circuit was increased in the proportion of 20 to 40 cm. of spark between the points of the gap-meter, which is equivalent to 100 or 180 kv., and even 200 kv. and more. The Coolidge tubes were perfected so that they could support these high potentials with an increasing intensity from 2 to 5 ma. The filters from 5 to 15 mm. of aluminum, which were in use up to 1922, were subsequently replaced by zinc or copper varying in thickness from 0.5 to 2 mm. and increased by 3 mm. of aluminum. During this same period the focal distance was increased from 20 to 50 cm. and even 60 to 70 cm., thus diminishing the difference between the cutaneous doses and the doses in the depth.

Thus we note that between the years 1923 and 1928, during which period the successful cures reached a percentage of 39, we made use of a potential of 180 to 200 kv., an intensity of 3 to 4 ma. on the secondary circuit, a filtration of 2 mm. of zinc and 3 mm. of aluminum, and an anticathode skin distance of between 50 and 70 cm. In the

years previous to 1923, when one noted only a series of failures, these factors had varied below the amounts just specified. It therefore seems without doubt that, directly or indirectly, the quality of rays is of some importance in determining the success of roentgen therapy.

NUMBER AND SURFACE OF THE AREAS IRRADIATED

In order to restrict diffusion and give more direct irradiation to deep neoplastic elements, some radiologists are using small but numerous cutaneous portals. Other radiotherapists believe in the advantage of less numerous but larger areas. By so doing, they wish to make use of scattered rays, and distribute the doses more equally. Thus, the primary tumor and neighboring glands are flooded in the same cone of rays, which is an added advantage. Of course, it is known that more intensive generalized reactions are observed with the use of the larger portals.

Between the maximum area of 352 cm. and the minimum area of 40 cm., we have registered all those other intermediate sizes.

No doubt the small fields of irradiation have given very unfavorable results. Two cases may be herewith reported to demonstrate this point. The first case was an ulcerated lymphosarcoma of the cavum which recurred after radiotherapy and occupied the whole pharynx down to the epiglottis, with a certain amount of adenopathy in the right and left submaxillary region. Roentgen therapy was applied in 10 fields of 50 cm. over the mastoid, maxillary, cervical and buccal regions; the total dosage was 102 H spread over twenty-five hours and forty-five minutes in the course of 28 sittings given at intervals in a twenty-seven day period. A rest of ten days during the treatment was necessitated by local and generalized reactions. There was a rapid disappearance of the pharyngeal tumor. One gland in the submaxillary region persisted. Recurrence in the cavum was noted after six months and death by generalization of the condition occurred ten months and a half after the beginning of the treatment.

The second case was a lymphosarcoma of the right palatine tonsil with a small mastoid gland. Bilateral roentgen therapy over seven fields of 40 cm. on the mastoid, submaxillary, laterohyoidal and anterior buccal regions, was given with a total dose of 110.5 H in thirty-seven hours and fifteen minutes, applied in 38 sittings, over a period of forty-one days. Marked local and general reactions necessitated the interruption of the treatment at intervals. There occurred a metastasis in the right knee and abdomen in less than six months, and the patient died one year and fifteen days after the beginning of radiotherapy.

In these experiments which have not been repeated, the small fields have not prevented local or general reactions, and doses of 102 and 110.5 H have not brought about any cure. Of course, when extensive surfaces have been irradiated, the success has not always been complete. Nevertheless, among the 16 patients still considered as cured, 7 have been irradiated on cutaneous areas varying from 190 to 300 cm^2.; the 9 others surviving have been irradiated over areas no smaller than 100 cm^2. Even in cases where lesions are strictly unilateral, it is recommended that both sides of the neck and pharynx be irradiated, not only to have the benefit of crossfire, but also to prevent one or the other part developing a latent adenopathy.

However, among the 16 patients who were considered cured, 7 received only unilateral irradiation; 4 of these had no adenopathy and the other 3 had infiltrated lymph nodes on the same side as the pharyngeal lesion.

Among the 9 patients who have been cured with bilateral irradiation, 3 had no palpable lymph glands, 2 revealed infiltration of lymph glands on one side only, and 3 had very small bilateral adenopathy.

QUANTITOMETRY

In the treatment of all cases, the quantities of roentgen rays were measured by the

aid of barium platino-cyanide tablets on the skin. Doses were established by a colorimeter scale and expressed in Holzknecht units (H). It was not until 1928 that the ionometric apparatus of Solomon, Dauvillier, Bruzau, Ferroux, and Hammer were employed in the daily practice of roentgen therapy. The comparative studies by Coutard have led to the opinion that there is a close agreement between the Holzknecht unit which he observed and 100 r as defined by Behnken. It is therefore easy to transform the units of the old notation by multiplying them by 100 so as to obtain the roentgen equivalence; but, as Coutard has emphasized, this equivalence may be convenient but is not absolutely exact. When the field is small, that is when one tends to suppress the scattered rays, the Holzknecht unit seems less than 100 r; on the contrary, when the field to be irradiated is as large as 300 or 400 cm^2., 1 H corresponds to more than 100 r.

A ten-year cure was obtained with 12.5 H (1,250 r). In 2 other living patients, the dosage used was 74 and 65 H (7,400 and 6,500 r). On the other hand, some doses as high as 110 and 102 H (11,000 and 10,200 r) brought about only slight and transitory improvement. Between such extreme limits the quantities of roentgen rays have varied greatly.

When large extensive unilateral fields are irradiated, the most useful doses seem to be between 30 and 40 H, that is about 3,000 and 4,000 r; but when bilateral portals are used, 45 H (4,500 r) seems to be most efficient and harmless.

ORDER OF IRRADIATIONS

Large roentgen doses should be extended over a long period so as to prevent local complications resulting from a too intensive treatment. One should beware of serious general reactions which are oftentimes the outcome of too rapid disappearance of the lymphosarcoma. Nevertheless, we have seen 2 patients cured after receiving on one side of the neck 45 H, applied in five and ten days. In 1 case, four daily sittings were sufficient for definite cure, whereas, in the other case, 24 sittings over a period of sixty-two days gave the same end-result.

Between these limits, there is place for all modes of repartition; nevertheless, the accumulation of facts leads one to believe that the best method of roentgen therapy in lymphosarcoma of the pharynx consists in a noninterrupted series of applications made once or even twice a day, on alternating sides of the face and neck, with progressively increasing doses until the total amount of 4,500 r has been obtained in three or four weeks.

BIOLOGICAL CONTROL

Roentgen rays produce on epithelial tissues of the mucous membranes and teguments certain definite reactions. These are useful to the therapist in determining the verification of the physical quantitometry. We are not considering here the cutaneous erythema (skin unit) nor the lethal dose for sarcoma (sarcoma dose), because both, as proposed by the German radiologists, lack a definite determination. I wish to discuss the radio-epidermitis such as described in 1913 by Regaud and Nogier, and the radio-epithelitis as described by Coutard in 1922.

It is important to know the effects of roentgen rays on the skin surface if one wishes to appreciate and control the action in the depth. Those biological reactions seem to summarize the influences which have provoked them and reveal objectively the efficacy of treatments.

In his studies of the results obtained with roentgen therapy on cancer of the larynx and pharynx, Coutard has noted with remarkable precision an example of radio-epidermitis, as follows: "Definite biological effects have been determined in the following physical conditions: focal distance 50 cm., irradiated area 50 cm.^{2}, curent intensity 4 ma.; 175 kv. constant potential, filtration 2 mm. of zinc. The effects obtained were the following: a dosage of 45 to 50 H (4,500 to 5,000 r) distributed during ten days, at a rate of two seances a day and of one hour duration, that is

twenty-four hours on the same lateral surface of the neck, causes on the twenty-sixth to the twenty-eighth day, a cutaneous lesion characterized by a desquamation of the epithelium, with an exposure of the dermis. Such a lesion should be repaired in fourteen days, that is, between the fortieth and the forty-second day, without leaving any apparent injury. This is the radio-epidermitis of Regaud and Nogier."

Where the dosage is increased, the tissue repair is retarded. If the dose is smaller, the scarring occurs sooner. The duration of repair indicates approximately the quantity of radiation which has been applied to the tissues.

Radio-epithelitis is to the mucous membrane what radio-epidermitis is to the cutaneous teguments. Due to the desquamation of the epithelium, the chorion is exposed and becomes covered with false membranes of a variable thickness which take on a diphtheroid aspect. In those physical conditions enumerated by Coutard, as we have noted, this radiation reaction begins to appear about the fourteenth day and is complete about the twenty-eighth day, at a period when radio-epidermitis will appear. At the beginning stage of the radio-epithelitis, the mucosa becomes red, smooth and varnished-like. Later, pearly blotches are seen and announce the coming denudation.

In most of our patients submitted to roentgen therapy, radio-epithelitis began at about the twentieth day of the treatment, while the cutaneous erythema and pigmentation announcing the approach of an epidermitis were observed between the twentieth and thirtieth day. The delay in these reactions may be ascribed to the particular protraction of doses.

Neither radio-epithelitis nor radio-epidermitis is a promise of local cure, although lymphosarcoma is, as a rule, more sensitive than the germinal layer of the epithelium. We have in our present statistics, two examples of local ill effects with radio-epithelial lesions.

It seems that the most convenient roentgen doses for treatment of lymphosarcoma are those which do not exceed the cutaneous lesions. The chances of success seem to be greater than with the stronger doses. Moreover, risks of accidents are thus diminished.

INCONVENIENCES AND COMPLICATIONS DUE TO ROENTGEN THERAPY

Certain local and general accidents, immediate or remote, may occur during or after roentgen treatment of lymphosarcoma of the pharynx. They are the same as those reported by Coutard concerning epithelioma of the tonsillar region, of the hypopharynx and of the pharynx.

Local Immediate Complications. These are rare and of no grave consequence, when the doses are less than those which should produce a radio-epidermitis; we have mostly observed dryness of the mucosa caused by a more or less lasting destruction of the salivary glands.

Late Local Complications. Apart from the chronicity of the preceding complications, in certain cases where radio-epidermitis was excessive, we noted some cutaneous atrophy with telangiectasia long after the treatment ended.

Dermitis occurred only twice: first, in a patient who received 62 H in twelve days; second, in a patient who presented a superficial necrotic spot more than two years after having received 74 H, over bilateral surfaces, in thirty-four days. These accidents are now less frequent with the use of modern dosimeters and a better knowledge of radiophysiology. In roentgen therapy of lymphosarcoma we stress the fact that epidermicidal doses are not necessary. It is only necessary to prevent or combat the secondary infection to reduce to a minimum the frequency and importance of the sequelae. Being more radiosensitive than others, lymphoid tumors do not require such intensive radiotherapy for their destruction. The complications therefore should not be of too great frequency or severity.

General Complications. General reactions

were observed such as fever, asthenia, gastrointestinal reactions with anorexia, nausea, vomiting and diarrhea. Taking everything into consideration, these phenomena appear in relation to the quantity of neoplastic cells and others which have been destroyed during the treatment. To prevent this inconvenience while one is maintaining the dimensions of the areas and their daily irradiations, it is only necessary to start with very weak doses and increase them progressively according to the resistance and behavior of the patient.

Autointoxication resulting from massive cellular resorption was once noted; cardiac disturbances followed which caused an interruption of the treatment.

CONCLUSIONS

Of all known methods of treatment of lymphosarcoma of the pharynx, roentgen therapy seems to be the most advisable.

By its use, Regaud, Coutard and coworkers in the Institute of Radium of Paris, have obtained 80 per cent immediate local cures and 34.8 per cent survivals of five years and more.

The involvement of the lymphatic system is the most important clinical factor in determining the prognosis.

Roentgen therapy in lymphosarcoma is more effective if protracted according to Regaud and Coutard's principles: long focal distance, well-filtered rays, large bilateral fields, hourly weak dosage and daily exposures.

The total dosage may cause a radioepidermitis but will not go beyond it. General and local complications due to roentgen rays are thus rarely of importance.

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A STUDY OF BACK-SCATTER*

By EDITH H. QUIMBY, M.A., L. D. MARINELLI, M.A., *and* J. H. FARROW, M.D.
Department of Biophysics, Memorial Hospital
NEW YORK CITY

THE radiation which is scattered back to the skin by the underlying tissues is an important factor in roentgen therapy. Many measurements of this radiation have been published; these differ considerably among themselves. The method ordinarily used has been first to measure the intensity of the beam of radiation in air, by means of a thimble type "air wall" ionization chamber, and then to measure the intensity of the same beam with the chamber on the surface of a phantom, at the same distance as in the first case. The difference between the two readings represents the back-scatter; it is usually expressed as a percentage of the primary, or air, value.

Possible Sources of Error in Thimble Chamber Measurements. The thimble chambers are calibrated against standard air chambers, found to be independent of wave length within a certain range of quality, which usually covers the entire range of the primary radiation studied, and assumed to be so throughout the entire range concerned, including the very soft components of the back-scattered radiation. Since these calibrated chambers presumably all agree when used in air, it is evident that there must be inherent errors either in their use or in their construction, to cause the obtaining of different results on the phantom. Sources of error are of two types, those due to the shape and size of the chamber, and those due to the material of which it is made. Some of those of the first type are indicated in Figure 1. The radiation which is effective in producing a reaction in the skin is that which is absorbed in a thin region at the surface of the body, such as in indicated by the dotted section of the figure. The ionization chamber should, then, measure just this radiation, no more and no less. The chamber is usually placed so that it is half submerged in the phantom, as indicated. Evidently the rays it should measure are those absorbed in a narrow portion of its volume, through the center. However, some are effective in its upper and lower portions which do not pass through the region referred to. Moreover, some of those entering the lower half of the chamber are

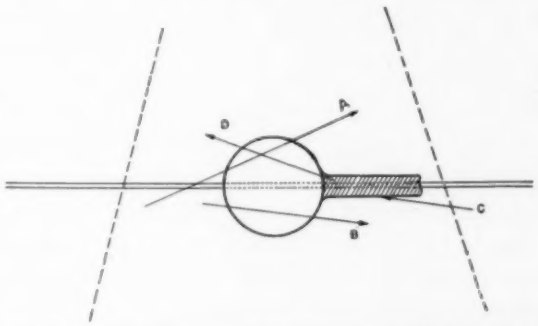

FIG. 1. Diagram indicating some sources of error in thimble chamber measurements of skin dose. The ionization measured should have the same average value per cubic centimeter as that actually existing in the space between the dotted lines. *A*, ray registering entirely in part of the chamber outside skin; *B*, ray scattered through less than 90°, which would never reach the skin; *C*, ray cut off from ionized volume by stem of chamber; *D*, ray originating in stem of chamber.

scattered through an angle of less than 90 degrees, so that they would never reach the skin. On the other hand, some of the rays which would reach the skin are cut off by the stem of the chamber, while some reach the chamber which originate in the stem instead of in the phantom. It is by no means certain that the average ionization per cubic centimeter produced in the entire chamber under these circumstances is the same as the average in the central zone. These difficulties would be lessened, but not eliminated, by using small chambers with very thin stems. The excess radiation

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reaching the chamber by the paths indicated is greater for hard than for soft rays, thus leading to high values for the back-scatter with increasing penetration of primary radiation.

Errors of the second type mentioned above are generally known as "wall effect." They are of two sorts, one due to actual absorption of radiation within the wall, and one to the emission of secondary radiation from it, of a somewhat different quality from that originating outside the chamber and absorbed by the wall. Within the limits of the experiments to be reported the effect due to absorption of radiation in the wall is essentially the same for both the primary and secondary radiation, and need not be considered. The effect due to emission of secondary radiation from the inner lining of the chamber (a coating of India ink) cannot be disposed of so simply. For the very soft components of the scattered radiation, the emission of photo-electrons from this carbon layer might be expected to assume some significance. It is sufficient to state at this time that this appears not to be the case, for the experiments here presented. Full details regarding this matter will be presented in a later publication from this laboratory.

It should also be mentioned that any metal parts in the beam (stem of chamber, connections to electrodes) may give rise to undesirable secondary radiation.

All the factors mentioned may assume different significance for different qualities of primary radiation and for chambers of different size, shape, material and construction. They probably account for some, if not all, of the divergences among published values for back-scatter.

In spite of all these possible sources of error, it is not certain that careful measurements with a good thimble chamber give wrong results. The errors may be too small to be significant, or they may average out. It is simply not certain that such measurements give correct results. It is necessary to compare them with others made under conditions which avoid those sources of error, and introduce no new ones.

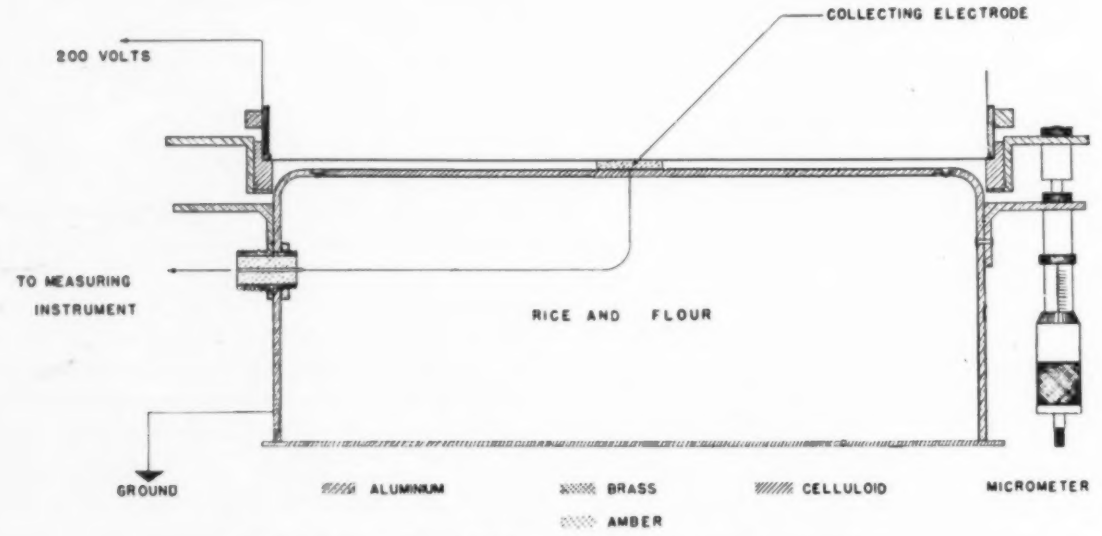

Fig. 2. Diagram of the Failla extrapolation ionization chamber.

The Failla Extrapolation Chamber. The extrapolation type of ionization chamber designed by Failla, and shown in Figure 2, is well adapted to such measurements.[1] This is a parallel plate chamber. The lower electrode is continuous with the phantom,*

* In the model used for the experiments herein reported, the lower electrode was actually the central portion of a sheet of celluloid 3 mm. thick, forming a cover over a tightly filled box of rice and flour.

the upper is mounted on micrometer screws so that the spacing between the two can be varied and accurately measured. This upper electrode is completely demountable, and the chamber is provided with several interchangeable ones of different thicknesses of organic material. The one normally used in the study of back-scatter is of parchment 0.2 mm. thick, but for very soft primary beams one has been used which is made of very fine silk net, having an average or effective thickness of 0.02 mm. In either case, electrical conductivity is obtained by painting the electrodes with India ink. Since there is no chamber wall whatever in the path of the back-scattered radiation which leaves the surface obliquely and enters the chamber, and since, as has been stated, the lower wall is effectively continuous with the phantom, there can be no wall effect due to shape or thickness of wall material, The possibility of an effect due to photo-electrons from the carbon is the same as with the thimble chamber. Their importance in the present work is discussed below. No part of the chamber is submerged so as to receive rays scattered through less than 90 degrees, and no part of it extends higher above the phantom than the rest; its whole thickness can be made comparable to the skin layer. There are no parts to cast shadows, and no metal parts to generate unwanted secondary radiation.

The quantity to be determined in measurements of the type under discussion is the ionization per cubic centimeter (or per gram) of air. It is therefore necessary to know accurately the volume of the ionization chamber. The effective volume of the thimble chamber is found by comparing its reading with that of the standard air chamber for a known volume. Throughout the range of the quality in which the thimble chamber volume determined in this way remains constant, this chamber is independent of wave length. The existence of a wall effect for soft radiation is demonstrated by obtaining a change in effective volume. The volume of the extrapolation chamber can be obtained by direct measurement. The area of the electrode is known, and the plate separation can be determined. However, this determination is rather difficult for reasons which need not be discussed here. It is, moreover, a simple matter to measure directly the ionization per cubic centimenter, regardless of the actual spacing of the electrodes. This is accomplished by taking a series of ionization readings as the plate separation is varied in constant steps. Since the area of the collecting electrode is 6.85 sq. cm., the increase in volume for an increase of 1 mm. in spacing is 0.685 cc. The increase in ionization with such an increase in volume is the ionization in 0.685 cc. of air. With the plates separated just sufficiently to avoid actual contact (about 0.5 mm.), the first reading is taken. As separation is increased in 0.5 mm. steps, it is found that for the same volume increase, the same ionization increase occurs, up to a separation of several millimeters. The correct value of the ionization per cubic centimeter is obtained by dividing the increase in ionization for a given increase in volume by the volume increment, within this range.

(It should be mentioned at this point that the fact that the same increase in ionization is obtained for the same increase in chamber volume, from very small to relatively large total volumes, indicates the absence of a significant wall effect due to the India ink coating, in this case. If photoelectrons from the wall contributed an important part to the ionization, this contribution should vary as the plate separation was changed. However the ionization *per cubic centimeter* remains constant within the limits described.)

Experimental Procedure. The object of the study reported in this paper was twofold: to obtain accurate values for backscatter over a wide range of qualities of radiation, and to investigate the extent of the errors involved in making back-scatter determinations with thimble chambers. Accordingly, parallel series of observations were made with the two chambers. All

measurements were made with great care. Every series of experiments was repeated at least twice, and any failure of two sets of readings to check within less than 1 per cent was carefully investigated. Each of the special problems discussed below was investigated separately, rather than by calculating from data already accumulated.

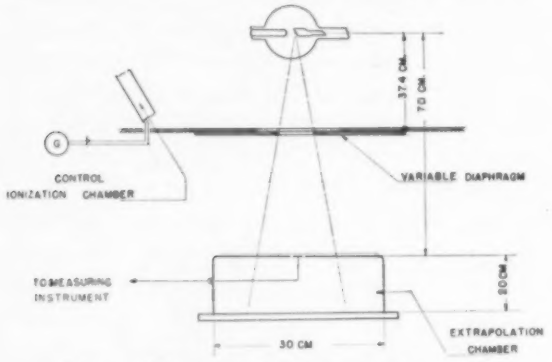

Fig. 3. Diagram of experimental set-up.

This plan, although involving considerable duplication of experimental work, assured that all data regarding any specific point were taken under the same experimental conditions, and contained no unnoticed error due to changes in atmospheric, electrical, or other conditions.

The sources of roentgen rays were air-cooled Coolidge tubes, housed in a lead tube holder 90 × 90 × 190 cm. in size, for all experiments except the distance effect with soft rays, when a special low voltage outfit was employed. For the harder rays the standard thick glass high voltage tube was used, for the softer, a thin tube. A diagram of the experimental set-up is given in Figure 3. Great care was taken to avoid extraneous scattering, and to be certain of the diaphragm sizes. A fixed ionization chamber in the tube holder, connected to a galvanometer as shown, gave continuous indication of the output of the tube. This output could be kept constant by means of an adjustable rheostat in the primary circuit and another in the filament circuit. Throughout the experimental work, one operator maintained the roentgen-ray voltage and intensity at fixed values, while another made the ionization readings. The Failla vacuum tube measuring device was used for the measurements.[2] Since this permits the instantaneous determination of the ionization current, each measurement could be made at an instant when the control instruments showed the correct values. The use of this apparatus also made it possible to make many observations in short periods of time, so that, in any given experiment, variations due to changing atmospheric or other conditions could be kept at a minimum, and many check readings could be taken.

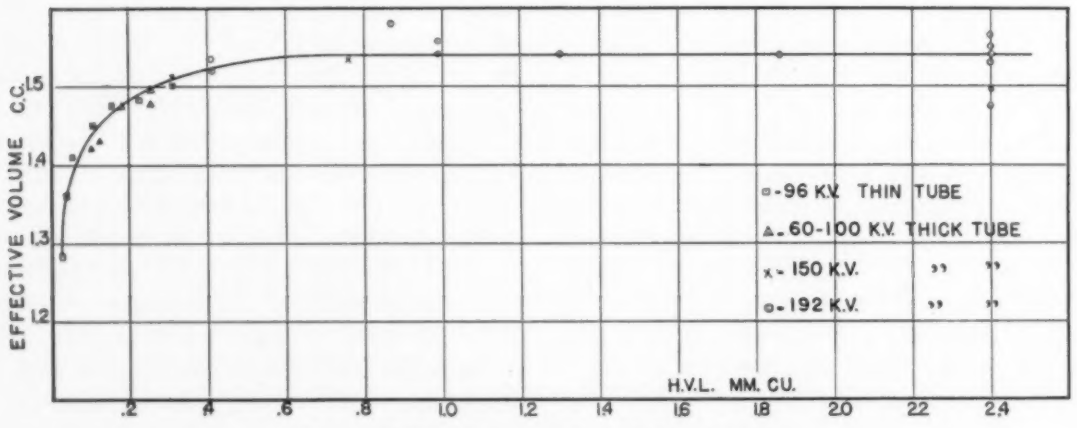

FIG. 4. Calibration curve for thimble chamber.

The range of radiation quality was from 192 kv. constant potential, filter equivalent to 5.0 mm. Cu, half-value layer 2.4 mm. Cu, down to 96 kv. unfiltered (thin tube), half-value layer 0.03 mm. Cu, or 1 mm. Al.

With the thick tube the voltage was carried down to 60 kv., at which point the half-value layer was 0.1 mm. Cu. The half-value layers were, in all cases, determined by absorption measurements with an air chamber. The various combinations of voltage and filter actually used will appear in the data below.

extrapolation chamber, the absorption of the rays in the corresponding thickness of wall material,—for the chamber in question, 1.4 mm. of celluloid.* For the softest quality of primary radiation used in this study, this effect amounted to about 15 per cent of the primary beam. This is to be interpreted that, if there were no absorption

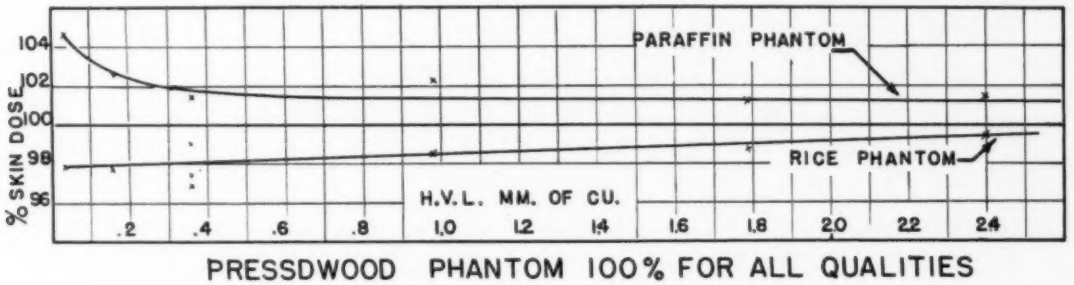

FIG. 5. Curves for relating back-scatter data from rice or paraffin phantoms to a pressdwood standard.

The thimble chamber was a celluloid sphere, 1.54 cc. in volume, with a wall thickness of 1.4 mm., attached to a brass stem 4 mm. in diameter. It was calibrated against the standard air chamber throughout the range of quality, for the measurements of the primary beam; the calibration curve is shown in Figure 4. As has been stated, the result of the wall effect for soft rays is to produce a change in the effective volume, in this case to diminish it. There is evidently no wall effect down to a half-value layer of 0.5 mm. Cu; below this it begins to appear. This is not a particularly wide range of wave length independence. Better chambers in this respect are available, but even in the best there will be a deviation of this type at some point, as softer radiation is used.

Since the wall effect of a thimble chamber consists of two parts, that due to absorption (and some scattering) of the primary beam, and that due to the emission of photo-electrons from the inner coating, the relative importance of these two factors in a particular case should be investigated. An approximation to the absorption in the wall can be found for any quality of radiation by measuring, with the and scattering of this sort in the wall, the end point of the calibration curve (toward the soft extreme) would be a little more than 15 per cent higher. This would mean that it would deviate less than 3 per cent from a straight line throughout its extent. In this case, very little effect could be attributed to photo-electric emission from the India ink lining.

For the experimental determination of the back-scatter, measurements of the primary beams in air were made with the thimble chamber. For every quality, the ionization per cubic centimeter was obtained, using the calibration curve of Figure 4. Measurements of the total radiation, including back-scatter, were made with the thimble chamber half buried on a pressdwood phantom, and with the extrapolation chamber with its rice phantom included. In order to make a satisfactory comparison of the two chambers, however, the same phantom material should be used. Subsidiary experiments were performed to determine the correction factor to be applied to

* The actual wall thickness is, of course, the *minimum* thickness traversed by any ray. Any which do not strike the surface of the chamber normally must pass through a greater amount of material. Hence the actual absorption is somewhat more than would be indicated by the air chamber measurement.

the rice phantom values for this purpose. (Correction was made to a pressdwood standard rather than to a rice standard since the former has been found the most satisfactory phantom material, and will be used in future measurements.) The correction curves are given in Figure 5.

The radiation due to the primary beam in each case was taken as 100 per cent. The total radiation was calculated in percentage of this primary, and the value of the back-scatter obtained by subtracting the primary from the total. The back-scatter is therefore given in terms of percentage of the primary radiation.

It should be mentioned that some individuals have preferred to express the back-scatter as a percentage of the *total* radiation. It may be pointed out that, in therapy, the quantity desired is the total radiation. If this could be accurately measured, under the conditions of treatment, a knowledge of the magnitude of the back-scatter would not be important in this connection. At present, however, there is considerable diversity in results obtained in measuring total radiation. On the other hand, accurate measurements of the primary beam are possible. For this reason, the convention has been established (in America, at least) that calibration, or standardization, of roentgen-ray beams shall be based on measurements of the primary beam.[13] In order to obtain the total radiation, the appropriate value for back-scatter must be added to this. For this reason, the value of the back-scatter should be given as a percentage of the primary beam.

It is highly desirable to have unanimity among radiologists with regard to this matter. Values of the back-scatter expressed in terms of total radiation are, of course, definitely lower than those expressed in terms of the primary beam. Unless the method of

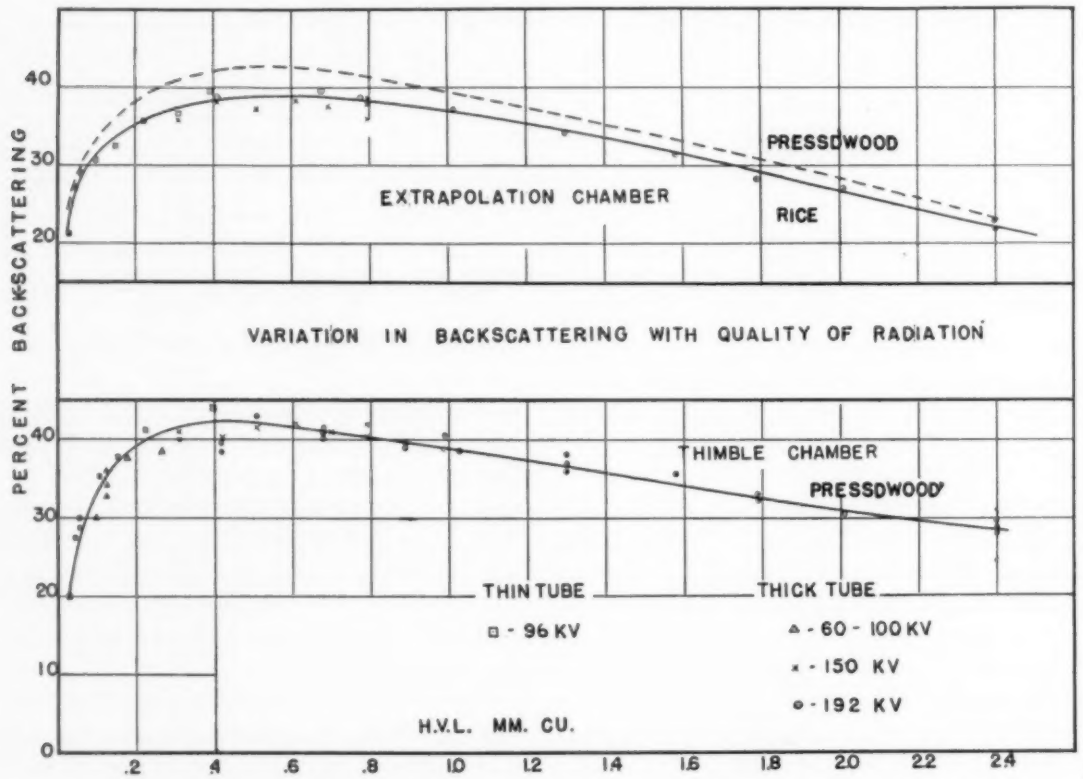

FIG. 6. Curves showing variation in back-scatter with quality of primary beam, for thimble and extrapolation chambers.

expression is always stated, or is established by convention, misunderstandings may readily arise as to which is meant.

Variation of Back-Scatter with Quality of Primary Beam. For the initial investigation of variation in back-scattering with quality, a constant field of 128 sq. cm. was used, and a constant distance of 70 cm. Figure 6 shows the results of this series of measurements, for both chambers. The solid curves show the actual experimental results; the dotted curve for the extrapolation chamber is the reduction to the pressdwood standard. The corrections applied to the rice phantom values were never more than 2 per cent of the total radiation (see Fig. 5). The quality of the radiation is indicated by its half-value layer in copper. The various voltages used to produce any quality are indicated, for the experimental points. It is evident that this specification of quality is sufficient in defining the back-scatter, for, within the range from 60 to 192 kv., radiation of a definite half-value layer gives the same back-scatter, regardless of the voltage and filter combination.

It is apparent that there is no radical difference in the shapes of the two curves. Figure 7 shows them superimposed, to bring out the variations between them. In the region of maximum back-scatter, the two chambers agree; as the radiation becomes harder, the thimble chamber gives higher readings, while in the other direction it gives lower ones. For a half-value layer of 0.5—0.6 mm. Cu, the back-scatter is a maximum, 42 per cent for the field used. At the hardest radiation investigated the thimble chamber gives 28 per cent and the extrapolation chamber 21 per cent, a difference of 33 per cent in the back-scatter, and of 6 per cent in the total radiation. At the other extreme, the two chambers appear to be in better agreement. However, it should not be overlooked that for very soft radiation the wall effect of the thimble chamber is a significant factor, both in determining the primary and the total radiation. Since the effective volume of the chamber changes rapidly with the quality, small errors in determining the half-value layer may lead to serious ones in determining the back-scatter. It is probable that the agreement between these two chambers for this part of the curve is fortuitous.

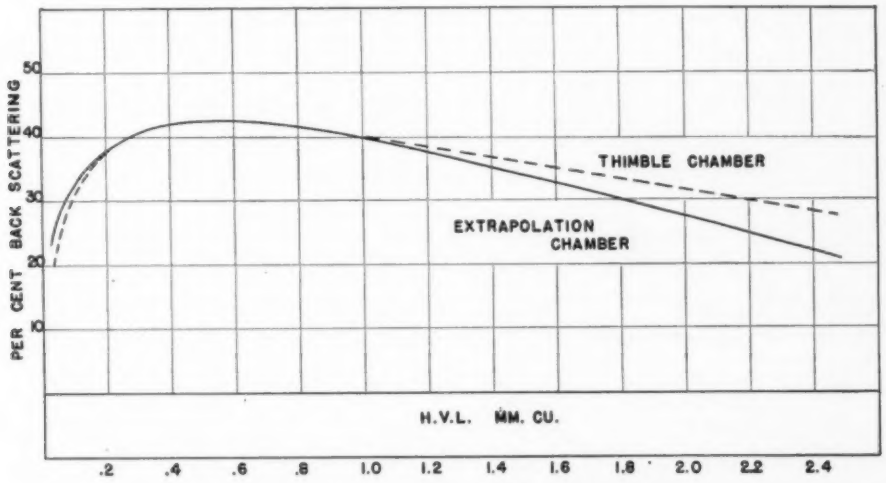

FIG. 7. Curves of Figure 6, superimposed for comparison.

As was stated, the curves just discussed were obtained with beams filtered by copper, and whose quality is expressed by half-value layer in copper. However, for low voltage radiation, aluminum is commonly used as the filter material, and the half-value layer may be specified in either this material or copper. Accordingly, for the radiation from the thin tube, from 140 kv.

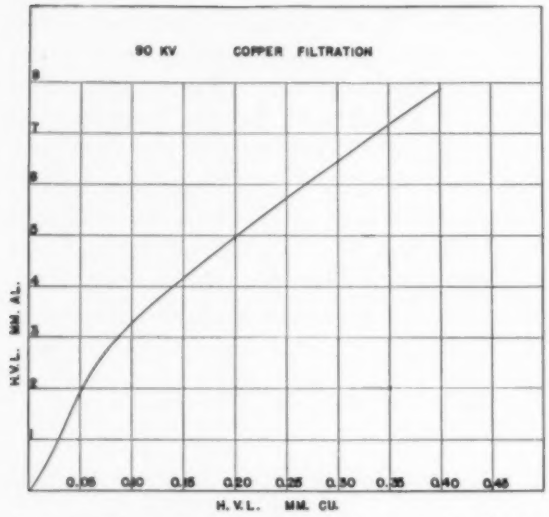

FIG. 8. Curve showing relation between half-value layers in aluminum and in copper for soft roentgen rays.

down, the half-value layer in aluminum was obtained for the copper-filtered beams. The relation between half-value layers in the two metals in shown in Figure 8. The back-scatter related to aluminum half-value layers is shown in Figure 9, experimental points for copper-filtered radiation being indicated by triangles and for aluminum-filtered beams by crosses. Deviations from the curve are of the order of 3 per cent, and may be attributed to experimental error. It is evident that, for radiation within the range investigated, half-value layer in either aluminum or copper is satisfactory as an expression of quality, so far as determination of back-scatter is concerned. From the point of view of using these curves, for soft radiation aluminum is more satisfactory than copper, since an error of even as much as 0.5 mm. in determining the half-value layer in aluminum gives rise to only a insignificant difference in back-scatter.

Variation in Back-Scatter with Irradiated Area. It is evident that, up to a certain point, the greater the irradiated area, the greater will be the back-scatter, since this scattered radiation comes not only from the region immediately beneath the ionization chamber, but from all the material surrounding this region. The variation with field will, within certain limits, be greater for hard than for soft rays, since the scattered hard rays can reach the chamber through a greater thickness of material.

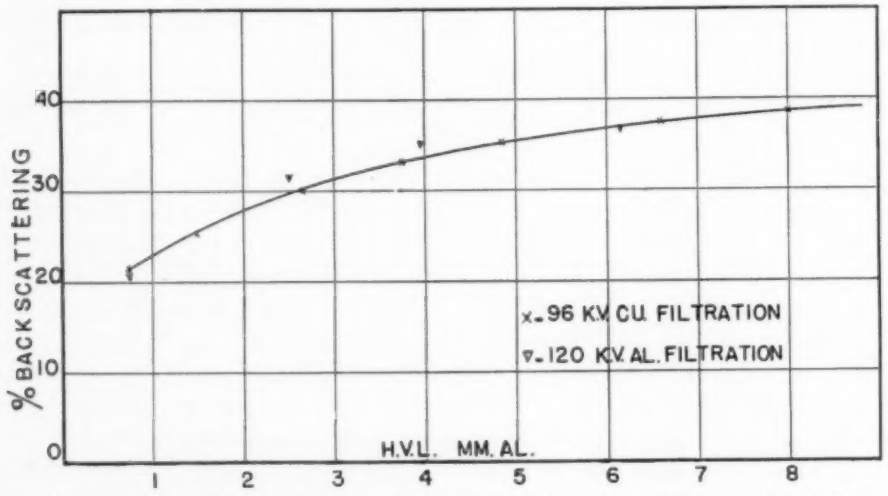

FIG. 9. Curve showing back-scatter in relation to half-value layer in aluminum for soft roentgen rays. (Pressdwood phantom, extrapolation chamber, 100 sq. cm. field.)

The effect of the size of field was investigated for several qualities of radiation, in each case by keeping the quality fixed (not even turning off the roentgen rays while adjusting the diaphragm) and varying the field within wide limits. In addition to making these measurements with both chambers on their phantoms, they were

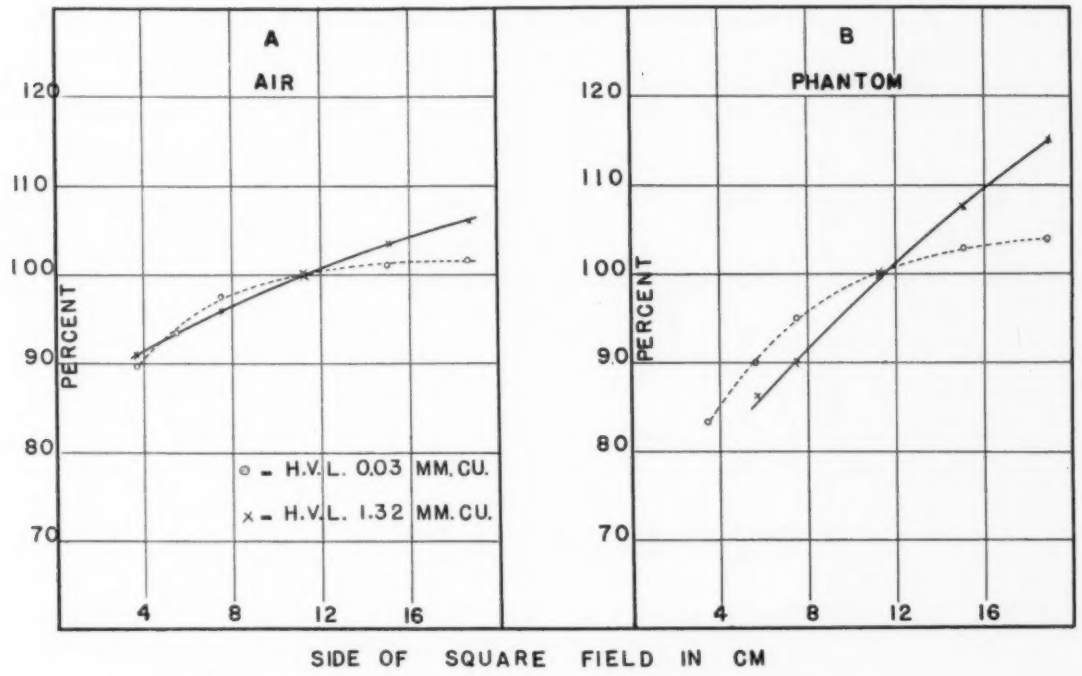

FIG. 10. Curves showing effect of field on back-scatter. *A*, measurements in air; *B*, measurements on phantom.

made for the thimble chamber in air. It should be emphasized that this is necessary in determining the actual back-scatter for different fields, since the intensity of the primary beam also changes with the diaphragm opening, due to the fact that the source of the rays is not a point, but includes off-focus radiation from the tube, and also scattered rays from the interior of the tube holder. Figure 10*A* shows the variation in air reading with the field, for two qualities of radiation; Figure 10*B* the variation in total radiation for the same qualities. In each case the radiation for a field of 128 sq. cm. is taken as 100 per cent, and that for any other field reduced to this basis. This field effect was found to be the same for the thimble and extrapolation chambers. The actual values for back-scatter, for a wide range of fields and qualities of radiation, are found in Table I.

Effect of Depth of Underlying Material. For the same reason as the variation with size of field, the back-scatter will vary with the depth of underlying material. That is, up to a certain depth, the more material there is to scatter, the greater will be the amount of scattered radiation. The maximum will be reached sooner for soft radiation than for hard. In all the preceding data it is assumed that there is sufficient underlying material to assure the maximum back-scatter for every quality of radiation. In therapy, however, it is often the case that this maximum is not reached. The question of the variation in back-scatter with depth of underlying material has therefore been investigated for different qualities of radiation, for large and small fields. The experimental results are shown in Table II, in terms of the percentage of the maximum back-scatter obtained for any specified thickness of material. They were the same, within the limits of experimental error, for fields of 25 and 200 sq. cm. The actual value for the back-scatter, when less than the maximum is obtained, is found by multiplying the maximum value, as given in Table I, by the indicated percentage.

Variation in Back-Scatter with Target-Skin Distance. Certain investigators have

TABLE I

BACK-SCATTER FOR VARIOUS FIELDS AND QUALITIES OF RADIATION IN PERCENTAGE OF THE PRIMARY BEAM AS 100 PER CENT

Half-Value Layer		Area of Field—Square Centimeters									
Mm. Al	Mm. Cu	5	10	25	50	75	100	150	200	300	400
		Back-Scatter—Percentage of Primary Beam									
1.0	0.035	11	14	17	21	23	24	25	26	27	28
2.0	0.055	12	15	19	24	26	27	28	30	32	34
3.0	0.09	13	16	21	25	29	30	32	34	36	38
5.0	0.2	14	18	24	30	32	34	38	40	44	47
8.0	0.42	15	19	26	32	36	38	43	46	49	52
	0.5	15	19	26	32	36	38	43	46	49	52
	1.0	14	18	24	30	34	36	40	43	46	49
	1.5	11	15	20	26	29	31	36	38	41	44
	2.0	9	12	17	21	24	26	29	31	34	36
	2.5	8	9	13	16	18	20	22	24	26	27

reported variation in back-scatter with target-skin distance. It would appear that no significant variation should be expected, however the matter was investigated, for a range of distances which might be used in therapy, for hard and soft rays. It is not necessary to determine the actual back-scatter in such an investigation; it is simply necessary to find out whether the readings in air and on the phantom vary in the same ratio, provided the fields are kept the same. If they do, there can be no difference in back-scatter. Using roentgen rays at 192 kv., filtered by 1 mm. Cu, half-value layer 1.3 mm. Cu, the ratio between readings with the thimble chamber in air, and with the extrapolation chamber, were the same at at 123 cm. distance as they were at 61.5 (within less than 1 per cent) for fields of 100 and of 250 sq. cm. On account of the size of the tube holder used in these experiments, it is difficult to work with the extrapolation chamber at distances less than 60 cm. Earlier experiments with the thimble chamber and a paraffin phantom showed no difference in back-scatter with distance from 40 to 150 cm., over a wide range of fields, for radiation at 192 kv. filtered by 0.5 mm. Cu, half-value layer 1.0 mm. Cu. With roentgen rays at 100 kv. filtered by 2 mm. Al,

TABLE II

VARIATION IN BACK-SCATTER WITH DEPTH OF UNDERLYING TISSUE FOR DIFFERENT QUALITIES OF RADIATION

Depth of Underlying Tissue	Half-Value Layer—mm. Copper					
	0.03	0.05	0.1	0.2	0.4	0.5–2.5
cm.	Percentage of Maximum Back-Scatter*					
1	45	40	35	31	30	30
2	67	64	58	50	48	48
4	92	89	83	75	70	70
7	98	97	95	93	91	90
10	100	100	100	98	96	95
12				100	100	98
15						100

* Percentage of corresponding values from Table 1.

half-value 2.5 mm. Al, and the regular low voltage therapy installation, the ratios were the same at 31 and 66 cm. It seems evident that, within the range investigated, there is no variation in back-scatter with distance.

Comparison of Results with Those of Other Investigators. Little need be said about early measurements of back-scatter, since little is known of the characteristics of the chambers employed. Within the last decade, however, several extensive reports have appeared, in which the problem has been investigated in detail, with chambers which were said to be independent of the wave length of the radiation. Among these may be mentioned Glocker and Kaupp,[3] Rajewsky,[12] Jacobi and Liechti,[7] Gunsett and Nourettine,[6] Mayneord and Roberts,[8] Thoraeus,[14] Parker,[9] and Guében and Dumont.[5] The tables edited by Grebe and Nitzge[4] must also be mentioned. These do not report any individual experiments, but are the result of coördinating all the data available in the literature. They give a large bibliography, but do not mention the particular sources for the back-scatter data selected.

The eight separate researches just mentioned were conducted with attention to experimental details, and with precautions to avoid errors, yet the values they report for back-scatter for specified qualities of radiation, vary among themselves by more than 100 per cent! In Table III are given some of the values reported in the papers mentioned above, together with the thimble chamber values obtained in the present investigation. The values given by Grebe and Nitzge, and those obtained with the extrapolation chamber are appended for comparison.

The state of affairs set forth in this table is disturbing. It is difficult to see what variations in experimental set-ups could lead to the differences here found. Factors

TABLE III

VALUES OF BACK-SCATTER OBTAINED BY VARIOUS INVESTIGATORS. "AIR WALL" THIMBLE CHAMBERS. 300 SQ. CM. FIELD. 70 CM. DISTANCE.

Date	Author	Material of Phantom	Half-Value Layer—mm. Copper						
			0.1	0.3	0.6	1.0	1.5	2.0	3.3
			Back-Scatter, Percentage of Primary Radiation						
1927	Glocker and Kaupp*	Water		24	33	30	27		
1927	Rajewsky	Water		14	19	22	25		
1928	Jacobi and Liechti	Water	30	42	44		46		
1930	Gunsett and Nourettine*	Wax	43	58	67	63	58	54	40
1932	Thoraeus	Wax	40	54	53	52	49		
1933	Mayneord and Roberts†	Water		34	47	49	45	37	31
1935	Parker	Wax		70			52		34
1936	Guében and Dumont	Wax	47	57	61	52	46	40	
1937	Quimby, Marinelli, and Farrow	Pressdwood	38	48	49	47	43	37	
Average			40	45	47	45	43	42	35
Grebe and Nitzge			25	33	37	38	39		
Extrapolation Chamber (Pressdwood)			37	47	49	46	41	34	

* Calculated from value for 400 sq. cm.
† Calculated from value for 130 sq. cm.

which vary in different investigations are the use of air-cooled or oil-immersed tubes, construction of tube holders, position of diaphragms, presence in the beam of supports for diaphragms or phantom, material of phantom, etc. It is not always possible from the published report to determine the details of experimental set-up or procedure. Some investigators have determined their own half-value layers; others have taken them from the Grebe and Nitzge tables. Some of them have discussed in detail the calibration of their thimble chambers, others have simply stated that they were independent of the wave length. With the exception of Thoraeus, none discussed the variation in primary radiation with variation in diaphragm opening, and in some cases it is impossible to determine whether this has been taken into account.

With regard to the material of the phantom, Jacobi and Liechti have carried out an extensive study.[7] They found that paraffin and wax gave values of back-scatter markedly higher than water or rice (which agree very closely, and agree also with the values for tissue). This difference increases with increased softening of the radiation. The existence of a difference between paraffin and water has also been reported by one of the present authors.[10] In the course of the present investigation this was confirmed. A study of rice and of pressdwood as phantom materials showed that they agreed quite closely with water and with each other. In Table III it is to be noted that all values obtained with any form of wax fall into a group definitely higher than those obtained with water or pressdwood.

It is interesting to note that, in spite of all the discrepancies in absolute value of the back-scatter, all but three of the papers listed give a maximum in the region of 0.6 mm. copper half-value layer, which is in agreement with the data obtained with the extrapolation chamber.

The effect of variation in back-scatter with irradiated area as given in these papers was found to differ considerably. In some cases it was stated that the primary radiation was determined for the same field as the scattered; in others this fact is not mentioned. It has been pointed out that this is important. The field effect for the primary beam is dependent on the type of tube, tube holder, and diaphragm system. That for the scattered radiation, especially for large fields, will also depend to some extent on the phantom material.

The effect of depth of underlying material was investigated in three papers; two report results essentially the same as those of the present authors. The third found an increase in back-scatter with thickness of underlying material even up to 60 cm. of wax. Since such a result has not been found by others, and is hardly justifiable on theoretical grounds, it would seem that it must be due to some spurious effect.

A variation in back-scatter with target-chamber distance is reported in two cases. Three others investigated the question and found no variation, this being also the experience of the present authors.

It is of interest to note that all investigators who related back-scatter and half-value layer in copper agreed that the same scatter was obtained with radiation of the same half-value layer, regardless of the voltage and filter combination used.

Critical mention may be made at this time of a previous paper by one of the present authors, with other collaborators, in which measurements of back-scatter made with a chamber of the mesh type were presented.[11] The values there given are considerably greater than those in the present paper, and show no definite maximum in the region of half-value layer 0.6 mm. copper. In this work the ionization chamber consisted of three parallel electrodes of fine silk mesh; the back-scattering phantom was a large pot of paraffin which could be brought close to the chamber or removed entirely. The primary beam and the total radiation including back-scatter were measured with the same chamber. As has been stated above, the use of paraffin as a phantom material results in high values for back-scatter, particularly for soft radia-

tion. In addition, the experimental set-up introduced other sources of error, which need not be discussed in detail, but all of which operated in the same direction, to give too high values for the total radiation, and hence for the back-scatter.

With regard to the lack of a maximum in the back-scatter at some particular quality, several factors should be considered. It has already been mentioned that the use of paraffin as the phantom material tends to bring values for soft radiation to a higher level in proportion than for hard. However, other workers have found a maximum even when using wax phantoms, so that this is probably not the determining factor.

The curve in the earlier paper relating back-scatter and quality is definitely flat for soft radiation. The experimental points are rather scattered, and the group for any particular kilovoltage might be interpreted as showing a tendency to decrease toward soft rays. If this trend were taken into account, a maximum would appear at about half-value layer 0.3 mm. Cu, which is softer than the quality for the maximum given in the present paper, or obtained by other investigators. It is obvious that there must be a maximum somewhere, for the back-scatter must come to zero at the limit of half-value layer equal to zero. Hence if the curve should actually be flatter than the present measurements show, it must ultimately come down more steeply.

It must be emphasized that it is not the desire here to discredit the above discussed work. It was, so far as has been ascertained, the first attempt to measure back-scatter by an ionization method which avoided some of the difficulties of thimble chambers. It apparently introduced others, some of which have now been found to be avoidable. The measurement of primary and scattered radiation by the same chamber, which is in both cases an air chamber, is extremely desirable, and is a feature which it has not been possible to preserve in the present work. This is, in other respects, an improvement and a refinement on the earlier method, eliminating the difficulties due to lead diaphragms near the chamber and scattering mass, and to an unduly large ionization chamber, and substituting a tissue-like substance for paraffin. Due to factors already discussed, the values now given represent more accurately the back-scatter within the region of radiation ordinarily used in therapy. However, it must be concluded that, for the extremely soft rays, the evidence at hand is not sufficient to settle the question. It is necessary to carry out a thorough investigation of chamber material and phantom material for radiation of half-value layer less than 0.25 mm. Cu.

The Usefulness of Thimble Chambers in Determining Back-Scatter. As has been already pointed out, values obtained with the extrapolation chamber do not differ much from values *obtained under the same experimental conditions, with one particular thimble chamber,* except toward the extremes of quality in both directions. The deviation of any other thimble chamber from the extrapolation chamber will not, of necessity, be the same as that of the one used in these experiments. As a matter of fact, it would be surprising if one different in shape and construction gave the same results.

For any particular thimble chamber, a calibration can readily be made against a chamber of the extrapolation type, to determine its error. Throughout the range in which the difference in total radiation recorded by the two is only a few per cent, there is no objection to using the thimble chamber for purposes of dosage measurement. Great care should be exercised, however, to see that it is not used for qualities of radiation for which it has not been calibrated, especially if its values are diverging from the standard at all rapidly. As a matter of fact, it is probably preferable to use the thimble chamber only to measure the primary beam. From the back-scatter data contained in this paper, or obtained in an equivalent manner, the value of the total radiation can be calculated for any quality of radiation, any field, and any distance,

within the usual limits of present day roentgen therapy (excluding "supervoltage")

The Determination of the Skin Dose in Roentgens. The skin dose is, of course, the sum of the radiation absorbed from the primary beam and from the back-scatter. There is at the present time a growing tendency to express tissue doses in terms of roentgens, in spite of the fact that the roentgen as at present defined is not strictly applicable for this purpose. Failla[1] has suggested that the tissue dose should be based on the ionization produced per gram of air, at the point where the radiation is absorbed, and under the conditions under which it is administered. If the actual number of ions chosen as the unit is

TABLE IV

SKIN DOSE IN "TISSUE ROENTGENS" RESULTING FROM THE ADMINISTRATION OF 100 ROENTGENS MEASURED IN AIR AT THE SAME DISTANCE

Depth of Underlying Material	Irradiated Area—Square Centimeters									
	5	10	25	50	75	100	150	200	300	400
	Low Voltage									
cm.	Half-Value Layer 1.0 mm. Al or 0.035 mm. Cu									
1	104	106	108	110	111	111	112	112	113	113
2	107	109	112	114	116	116	117	118	118	119
4	110	112	116	120	121	122	124	124	125	125
6 (max.)	111	114	117	121	123	124	125	126	127	128
	Half-Value Layer 2.0 mm. Al or 0.055 mm. Cu									
1	104	106	108	110	111	111	112	112	113	113
2	108	110	112	115	117	117	118	119	120	122
4	110	114	117	121	122	124	125	126	128	130
7 (max.)	112	115	119	124	126	127	128	130	132	134
	Half-Value Layer 3.0 mm. Al or 0.09 mm. Cu									
1	104	106	107	109	110	111	112	112	113	113
2	107	110	112	115	117	118	119	120	121	122
4	110	114	117	121	124	125	127	129	130	131
7	112	115	119	124	128	129	131	132	134	136
10 (max.)	113	116	121	125	129	130	132	134	136	138
	Half-Value Layer 5.0 mm. Al or 0.2 mm. Cu									
1	104	106	107	109	110	111	112	112	113	114
2	107	109	112	115	116	117	119	120	122	123
4	110	114	118	122	124	126	129	130	133	135
7	113	116	122	127	130	132	136	138	141	144
11 (max.)	114	118	124	130	132	134	138	140	144	147
	Half-Value Layer 8.0 mm. Al or 0.42 mm. Cu									
1	104	106	108	110	111	112	113	114	114	115
2	107	109	112	115	117	118	120	122	124	125
4	110	113	118	122	125	127	130	132	134	136
7	114	118	124	129	133	136	139	141	144	148
12 (max.)	115	119	126	132	136	138	143	146	149	152

Table IV—*Continued.*

Depth of Underlying Material	Irradiated Area—Square Centimeters									
	5	10	25	50	75	100	150	200	300	400
cm.	High Voltage									
	Half-Value Layer 0.5 mm. Cu									
1	104	106	108	110	111	112	113	114	114	115
2	107	109	112	115	117	118	120	122	124	125
4	110	113	118	122	125	126	130	132	134	136
7	114	117	124	129	132	134	139	141	144	147
10	115	118	125	130	134	137	141	144	147	150
15 (max.)	115	119	126	132	136	138	143	146	149	152
	Half-Value Layer 1.0 mm. Cu									
1	104	105	107	109	110	111	112	113	114	114
2	106	108	112	114	116	117	119	120	122	124
4	110	112	117	121	124	126	128	130	132	134
7	112	116	122	127	130	133	136	138	142	144
10	113	117	123	128	132	134	138	141	144	146
15 (max.)	114	118	124	130	134	136	140	143	146	149
	Half-Value Layer 1.5 mm. Cu									
1	103	104	106	108	109	110	111	112	112	113
2	105	107	110	112	114	115	117	118	119	121
4	107	110	114	118	120	122	125	126	128	130
7	110	114	118	124	126	128	132	134	137	139
10	110	114	119	125	128	130	134	136	139	142
15 (max.)	111	115	120	126	129	131	136	138	141	144
	Half-Value Layer 2.0 mm. Cu									
1	102	104	105	106	107	108	108	109	110	110
2	104	106	108	110	111	112	113	114	116	117
4	106	108	112	114	116	118	120	122	124	125
7	108	111	115	119	122	124	126	128	130	132
10	108	111	116	120	123	125	128	129	132	134
15 (max.)	109	112	117	121	124	126	129	131	134	136
	Half-Value Layer 2.5 mm. Cu									
1	102	103	104	105	105	106	106	107	108	109
2	103	104	106	107	108	109	110	111	112	113
4	104	106	108	111	112	113	115	116	118	120
7	105	108	111	114	116	118	120	121	123	124
10	106	108	112	115	117	119	121	122	124	125
15 (max.)	108	109	113	116	118	120	122	124	126	127

the number corresponding to the international roentgen in free air (3.24×10^{12} ions, or 1.62×10^{12} ion pairs per gram of air), then numerically doses specified in terms of this unit will be the same as in roentgens.

It is desirable, however, not to speak of tissue dosage measurements in terms of this unit as being made actually in roentgens, until the whole matter of dosage units is settled by international agreement. For

convenience, and for want of a better term, they may for the present by referred to as "tissue roentgens."

Measurements made with the extrapolation chamber can readily be converted into this unit. Hence the data thus obtained are directly applicable in the determination of skin doses. From the data of Tables I and II, these can be obtained for any irradiation within the range considered. In Table IV are given the skin doses, in terms of "tissue roentgens," resulting from the administration of 100 r, measured in air, for a wide range of qualities of radiation, fields and thicknesses of underlying material.

It should be noted that these skin doses are strictly applicable only to treatments in regions where the volume of back-scattering material is comparable to the phantom used. They are approximately correct for any case where the field is not almost as large as the part of the body used (e.g., for a very small field on the arm or a moderately small one on the neck). For fields almost as large as the part of the body, the actual skin dose will be somewhat less than the one given in the table.*

SUMMARY AND CONCLUSIONS

Sources of error in thimble chamber measurements of back-scatter are discussed.

Measurements of back-scatter are presented for a wide range of quality of radiation, of irradiated area, and of depth of underlying material, made with two types of ionization chamber. One of these is the ordinary "air wall" thimble chamber, the other the Failla extrapolation chamber, which is free from most of the errors inherent in thimble chambers.

Values obtained with the extrapolation chamber agree with those for this particular thimble chamber, from half-value layer 0.25 to half-value layer 1.1 mm. Cu. For harder radiation, the thimble chamber values become increasingly higher than those for the extrapolation chamber, while for very soft rays the thimble chamber values are lower. For this soft radiation, however, the differences cannot be considered as definitely established without further investigation of the wall effect in this region.

It is pointed out that these agreements and differences apply only to one particular thimble chamber; there is no way of generalizing from this particular instance.

With both chambers, the back-scatter is found to be a maximum for radiation of half-value layer about 0.5-0.6 mm. Cu.

For radiation of a given half-value layer in either copper or aluminum, the back-scatter is found to be constant, regardless of the voltage and filter combination used.

The variation in back-scatter with irradiated area is less for soft than for hard radiation. From half-value layer 0.5 to 2.5 mm. Cu, however, the variation between 5 and 500 sq. cm. is essentially the same.

The amount of underlying material necessary to produce maximum back-scatter increases with increasing hardness of radiation. This increase is rapid for soft rays, but very slow beyond half-value layer 0.5 mm. Cu. For radiation of this quality, maximum back-scatter is obtained with 15 cm. of underlying material.

The effect on back-scatter of changing the target-skin distance was investigated for soft and for hard roentgen rays. No significant variation was found for the soft rays for distances from 30 to 60 cm., or for the hard rays from 40 to 150 cm.

Results of other investigators published within the last ten years are tabulated and the variations discussed.

It is concluded that the values for back-scatter obtained with the extrapolation type of ionization chamber represent the best available at the present time, for radiation of half-value layer 0.25 mm. Cu to half-value layer 2.5 mm. Cu. For softer rays it is necessary to carry out further investigations regarding chamber and wall material; for harder rays no extrapolation chamber data are as yet available.

The applicability of these data to the de-

* An extensive investigation with small phantoms is planned. Data thus obtained will be published at a later date.

termination of skin dose is discussed. Extensive tables are given of the skin dose, in terms of "tissue roentgens," for a range of qualities from 0.03 mm. to 2.5 mm. Cu half-value layer, of fields from 5 to 400 sq. cm., and of thickness of underlying material from 1 to 15 cm.

It is pointed out that any thimble chamber can be calibrated against an extrapolation chamber and used, within the calibrated range, for dosage determinations. This is, however, unnecessary. Calculations from data of the type here published will, in general, be found more satisfactory and reliable than direct measurement.

We wish to express to Dr. G. Failla our appreciation for his suggestions and interest throughout the course of the work. We also acknowledge our indebtedness to Dr. A. P. R. Wadlund for his assistance in making many of the readings.

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METHODS OF APPLYING RADIUM ELEMENT IN THE FORM OF NEEDLES AND TUBES*

By GEORGE C. WILKINS, M.D.
MANCHESTER, NEW HAMPSHIRE

RADIUM element, as supplied for therapeutic use in needles and tubes, may be utilized for practically all purposes and in nearly every location and condition required. In some locations, particularly in the less accessible parts of the mouth, the difficulties associated with adequate and effective application are much greater than when using radon, and in many cases such adequate application becomes a greater tax on the ingenuity of the radiologist than the comparatively easy method of inserting radon seeds. It is impossible, however, for smaller hospitals, and in smaller communities, to have available the radium, the laboratory, or the personnel to supply emanations for daily use.

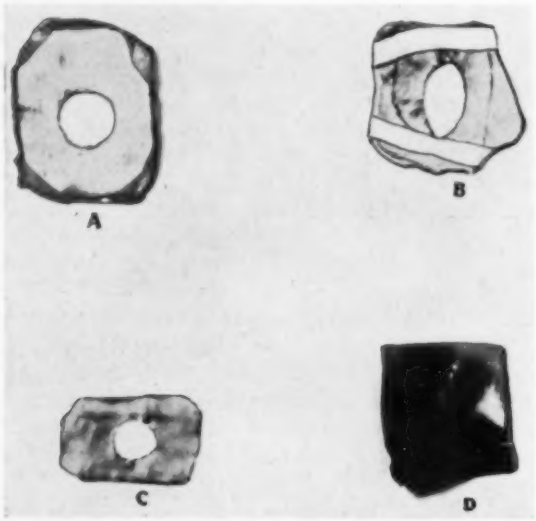

FIG. 1. Protecting screen for skin application. Lead 1 mm. thick; aperture 50 per cent larger than lesion; vulcanizing rubber next skin. *A*, shield ready to apply; *B*, one shield superimposed over another to make opening oval; *C*, lead with aperture; *D*, piece of vulcanizing rubber.

In 1920, when we began to use radium in the Elliot Hospital, one could only be guided by the methods and principles already developed in older and larger institutions. These were few enough for our purposes because the larger centers were using emanations. As patients with new and different lesions presented themselves, we were forced to improvise methods of application, and after many trials, and probably many errors, we gradually developed various technical procedures which have become routine in our clinic.

Those who use radium element exclusively are more inclined toward surface rather than interstitial application whenever adequate dosage may be administered in that way, on account of the ease of application, and the avoidance of tissue disturbance caused by the insertion of needles. Surface applications are made chiefly on the skin, the lip, and in certain locations in the mouth.

Our 200 milligrams of radium is divided in eight needles, containing 12.5 mg. each, and four tubes containing 25 mg. each. Four of the needles are of monel metal and four of platinum iridium, each with 0.5 mm. wall thickness. The tubes are two of silver and two of platinum iridium, with the same wall thickness. We also have one plaque 1.0 cm. square unscreened, with 2.5 mg. of radium. Our usual unit of treatment is 100 mg.

LESIONS OF THE SKIN

Surface applications are made with a group of needles and tubes wrapped in Para vulcanizing rubber 1/32 of an inch thick and the surrounding skin is protected by 1.0 mm. sheet lead, with an aperture in the center which is large enough to allow adequate exposure (Fig. 1). The aperture is fairly large for cancer but is cut accurately to size for nevi or angiomata. The surface of the lead protector next the skin is covered with the vulcanizing rubber to

* Read at the Twenty-second Annual Meeting, American Radium Society, Atlantic City, N.J., June 7–8, 1937.

screen out secondary rays and it also serves to hold the lead securely in place without slipping. Both shield and radium are held in place by strips of adhesive plaster. When treating superficial hemangiomata less than 1.0 cm. in diameter we use the plaque, and shield the surrounding skin with the thin lead used to protect dental films. This lead has an aperture cut the size of the lesion, as when using the heavier lead. More deeply seated and more extensive growths are treated by burying needles beneath the tumor and applying tubes to the surface, with a distribution that will deliver adequate crossfiring. Whenever needles are inserted or buried in tissue, a tract is first made by inserting the blade of a very narrow, straight cataract knife. This obviates unnecessary tissue trauma, for radium needles are never sharp, their diameter is about 1.7 mm., and they should never be forcibly inserted. It might be pointed out that the 25 mg. tubes are occasionally utilized for interstitial treatment, a tract being made with the cataract knife, which will allow easy insertion of the tube. The feel of this knife blade in the tissues is also of considerable aid in determining the extent of induration and fairly accurately defines the physical limits of the growth as well as indicating the best location for needle insertion.

Fig. 2. Cone-shaped lead shield with aperture in angle at inner canthus. Heavier lead over entire eyeball.

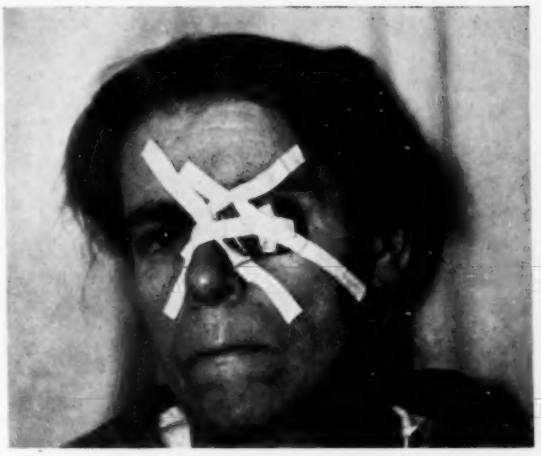

Fig. 3. Radium in rubber fastened over aperture in shield, and irradiating lesion.

Carcinoma of the skin near the inner canthus of the eye is frequently encountered and it is sometimes difficult to protect the eye and surrounding skin and at the same time make an adequate surface application, especially when the nose and the supraorbital ridge are prominent. We use a modification of the 1.0 mm. sheet lead with an opening large enough to give adequate exposure. A flat lead of the right size is cut through from the periphery to the aperture. When the cut edges are slid by each other, the lead assumes a cone shape which, by careful fitting, can be made to conform to the hollow between the eye, nose, and supraorbital ridge (Fig. 2). Here we make certain of close contact with skin and prevent displacement of the lead screen by using small strips of double faced adhesive on nose, cheek and lids, just before the screen is placed. The screen is held by strips of adhesive, an extra piece of lead is placed over the eye, and the radium, wrapped in vulcanizing rubber, is placed over the aperture in the shield (Fig. 3).

CANCER OF THE LIP

All cancers of the lip that have moderate, little, or no demonstrable induration are treated by surface application. The lead shield previously described, with an adequate aperture, is placed over the lip, the inner and outer edges of the lead squeezed

Fig. 4. Lead shield applied to lip, lip everted and lesion exposed through aperture.

as firmly toward each other as comfortably possible, the lip everted and held in this position by half-inch strips of adhesive (Fig. 4). The radium, again wrapped in rubber, is then placed over the aperture, practically in contact with the lesion and strapped in place (Fig. 5). Over this is placed lead to protect the upper lip, although the lower lip in eversion is not in close proximity to the upper. The patient has had a hypodermic injection of 1/100 gr. atropine sulphate, so a gauze sponge placed partly in the mouth, and changed at intervals, keeps the treatment area dry. Larger and more extensive lesions of the lip are treated by using two or three needles transversely beneath the growth, the lead shield over the lip, with an amply large aperture, on which is placed the surface application of the remainder of the radium. Lesions close to the angles of the lips require some modifications of this method, but the principles of application are the same.

Fig. 5. Radium in rubber placed over aperture and irradiating lesion. This in turn is covered with a 1.0 mm. lead shield.

LESIONS OF THE MOUTH

While we are using roentgen therapy more and more in cancer of the mouth, it still seems necessary or advisable in some cases to use radium. In the earlier days we used it on all cancers of the mouth, either alone, or in combination with electrocoagulation. Interstitial treatment may be used in the floor of the mouth, in the tongue as far back as the anterior pillars, and in the buccal surface of the cheek. In nearly all our mouth applications we have found the so-called "lead clamp" a most useful and efficient technical adjunct (Fig. 6). This clamp is fashioned out of sheet lead 1.0 mm. thick, using three layers of the lead wrapped in vulcanizing rubber. The clamp is approximately 15 cm. long, 2.5 cm. wide and the oral end is rounded or shaped to

Fig. 6. Lead clamp. Two to four pieces of 1 mm. lead, covered with vulcanizing rubber.

fit the particular need. If needles have been buried, this clamp can cover the area and protect the rest of the mouth. If it is desirable to combine interstitial with surface application, part of the radium may be fastened to the side of the clamp next to the growth, being strapped to the lead and covered with the rubber. Radium application to an alveolar ridge has always been difficult. By using this clamp, with the radium spread on the lead and covered with rubber, the clamp can easily be molded into the shape that will fit over the ridge without injury. That part of the clamp which protrudes from the mouth can be bent downwards or upwards, and firmly fastened to the lower or upper jaw with adhesive tape, and due to the thick lead shielding, only the lesion will be irradiated (Fig. 7). Other parts of the mouth are protected from irritation by the 3.0 mm. of lead. By arranging radium on both tips of the clamp and bending it in a U shape, a simultaneous external and internal surface application can be made to the cheek.

Lesions on the roof of the mouth or soft palate are best treated by surface applications, and the lead clamp properly applied to these locations will hold the radium firmly in contact. This can be done with very little manipulation and with a minimum of discomfort.

By using lead 1.0 mm. thick, one may easily cut the sheet to the desired size and shape with ordinary scissors, and the degree of shielding may be regulated by using as many similar pieces as seems desirable. This method of holding radium in the mouth, and for shielding radium has, in our hands, been found superior to the use of dental compounds, and requires less handling of the radium. Radium needles and tubes may be firmly attached to the lead surface by using double faced adhesive plaster.

METASTATIC LYMPH NODES

Primary oral growths with metastatic submaxillary, submental or cervical nodes are treated by roentgen rays, and the nodes are frequently treated subsequently with radium interstitially through an open incision. Occasionally a single submaxillary node close to the skin is treated by direct implantation through the skin without incision. Not infrequently we have a primary lesion in the lip or mouth with a small palpable node, usually just anterior to the submaxillary salivary gland, and in these patients the node, salivary gland and submaxillary node group are removed surgically. Before closing the wound radium in one or two brass cylindrical screens with a wall thickness of 1.0 mm. and enclosed in rubber drainage tube is placed in the wound, the wound closed except where the tube emerges, and the radium left in place for several hours. This method of treatment has been successful in properly selected cases.

Fig. 7. Lead clamp applied to left half of hard palate and alveolar area. Fixation by strapping to face. Several adhesive strips should be used.

CARCINOMA OF THE CERVIX

Patients with carcinoma of the cervix are given a preliminary series of deep roentgen therapy followed by radium irradiation. Our usual roentgen dosage is 1,800 r×5. When applying radium to the cervix, the radium needles and tubes are placed in brass cylindrical screens and the screens covered with the vulcanizing rubber. Before use the rubber covered screens are placed in crude carbolic for a few

minutes and then remain in alcohol until inserted. The patient is given ½ gr. of pantopon but no general anesthesia is used. Gentle dilatation of the canal is carried out with the graduated Hegar dilators. A brass tube screen containing 25 mg. of radium is placed above the cervix and one with 75 mg. in the cervical canal. The vagina is packed firmly with special gauze strips and a self-retaining catheter is placed in the bladder. The radium is removed in twenty hours. Forty-eight hours after the first treatment, a second is given for eighteen hours, but this time a T-shaped brass and aluminum screen is used with either 50 or 75 mg. in the shaft and the remainder in the cross piece. This is again held in place with packing. Two and a half weeks later a third treatment, usually by the first method, is given for eighteen or twenty hours. While this is the method used in the average case, various modifications are made in placing the brass screens when the individual condition indicates the desirability of different application. A variety of different sized screens makes this readily possible. For intrauterine treatment in patients with fibromyoma or with carcinoma of the fundus, we use two or three brass screens, either inserted separately or enclosed serially within a fairly thick-walled rubber tube, depending upon the size and conformation of the uterine cavity.

CANCER OF THE BLADDER

In cancer of the bladder the needles, and sometimes the tubes, are inserted into the bladder wall beneath the growth and all the threads on the needles are drawn through a small drainage tube which is long enough to extend from the group of needles up through the incision. When removed, all the threads and the tube with the attached needles are withdrawn together. Sometimes needles are placed beneath the growth and radium tubes enclosed in rubber are sutured over the surface with a running knot which can be released before removal of the radium. We usually give 1,200 to 2,000 mg-hr. in the bladder.

EXTERNAL DISTANCE APPLICATOR

Occasionally we wish to apply gamma radiation to a lymph node, particularly in the early tuberculous hyperplasias, or to some growth where long irradiation is indicated. For this purpose we use 100 or 200 mg. in several brass screens, each screen placed in a series of slots, 1.0 cm. apart, cut in a square or oblong of balsa wood about 1.0 cm. thick. A lead cap covers the radium and holds the screens in the slots. Between the wood and the skin is a 2.0 cm. layer of harness felt and the whole is wrapped in vulcanizing rubber. Greater distance may be obtained by utilizing a thicker layer of harness felt.

CANCER OF THE VAGINA

In the vagina it is sometimes necessary to treat various parts of the wall and at the same time protect surrounding areas. Many variations of the applicators, to fit all portions of the vagina from introitus to cervix, and with ample protection to areas not treated, can be improvised with the radium, lead and gauze packing, the applicator being always entirely covered with vulcanizing rubber.

VULCANIZING RUBBER

This has been mentioned several times and in our hands it has proved so useful and adaptable that it deserves a brief description and explanation. The rubber comes in rolls and is used by tire men for repairing inner tubes. It is soft, very flexible, easily handled and is very adherent to itself but only moderately adhesive to skin. Wrapping a group of needles or covering brass screens is very quickly accomplished by laying the group of needles or the brass screen on a square of rubber and folding the edges over each other with forceps until they adhere. The ends are pinched with forceps and the excess trimmed off with scissors (Fig. 8).

After trying many varieties of special forceps for handling needles, tubes and screens, we have discarded them all in favor of the so-called Russian dissecting

forceps (Fig. 9). This forceps has a rounded, rather blunt-toothed grasping surface which holds small and large objects securely and easily, and does away with the necessity of using an unnecessary number of special instruments. They are used for wrapping the rubber about the radium, holding it during application, and for all the ordinary procedures in which forceps are utilized.

This description of methods of applying radium element as carried out in a small hospital is necessarily brief, and while some of the apparatus may appear elementary, my associate and I have found the technique satisfactory in over 6,000 treatments in the past seventeen years. The simplest technical method that is efficient for a given purpose is usually the best.

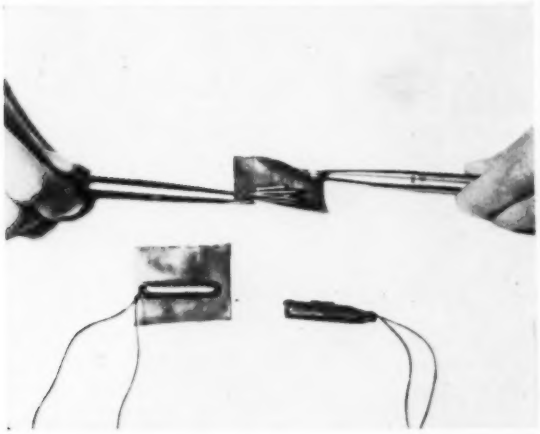

Fig. 8. Method of wrapping needles and tubes in rubber. Lower left, a brass screen containing radium about to be covered with rubber. Lower right, the same screen entirely covered with rubber.

Fig. 9. Russian forceps for holding and handling needles, tubes and screens. Applicable to all and will not slip.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Twenty-third Annual Meeting: Clift Hotel, San Francisco, Calif., June 13–14, 1938.

EDITORIAL

SANFORD MARTIN WITHERS
1891–1938

SANFORD WITHERS of Denver passed away at the Rockefeller Institute for Medical Research in New York City from aplastic anemia and bronchial pneumonia on March 8, 1938. He had been gravely ill for only about two months. From the obituary notice in the *New York Herald Tribune* of March 8, 1938, the following is taken:

Dr. Robert C. Fisher, Assistant Medical Examiner, said that Dr. Withers died of aplastic anemia and bronchial pneumonia. He added that there had been a "history of exposure to X-rays," and the physician who attended Dr. Withers disclosed that the progress of the anemia had been similar to that of known victims of excessive X-radiation. He fell ill of anemia last September, but did not become a patient at the institute until just after February 1st, when his condition became critical. At that time he told physicians that he had grown careless during the administration of treatments with new high-voltage apparatus, that he had exposed himself to scattered radiation, and that he soon afterwards had suffered from anemia.

Dr. Withers was a midwestern product. He was born in Clearwater, Missouri, in 1891; he graduated from the Manual Training High School at Kansas City in 1910 and received his medical degree from the Washington University Medical School at St. Louis in 1919. His interest in radiology developed at the Barnard Skin and Cancer Hospital at St. Louis. In 1921 Withers went to Denver as an expert and consultant for the Radium Company of Colorado. When the development of radium in the Belgian Congo dissipated the investments of this company in Colorado, he entered the private practice of radium therapy in Denver and continued there as a tumor specialist until his death. For many years he was Director of Radiation Therapy at the Denver General Hospital and he organized the Denver Tumor Clinic.

Dr. Joseph W. McKee, an ophthalmologist of Kansas City, was probably one of the most intimate friends of Sanford Withers. From Dr. McKee was obtained most of the information of the following paragraphs.

Very early in life, young Withers displayed a measure of genius and originality that lasted throughout his life. While still in the Manual Training High School he spent his summers and odd hours throughout the school year at the laboratory of Dr. Walter Cross, then city chemist of Kansas City. It is said that Withers did the first Wassermann tests in Kansas City. He also worked with Dr. Cross in the development of an oil cracking process which proved a great financial success for Dr. Cross. His academic years at Washington University were devoted to chemical engineering. This combination of chemistry, physics and medicine stood him in good stead when he began the practice of radium therapy. During the school years in St. Louis he was employed by the Mallinckrodt Chemical Company and in the laboratories of various physicians in St. Louis.

While still a senior at the Washington University Medical School, Withers and McKee went to France with Base Hospital No. 21, which was attached to the British Expeditionary Forces. Both served as ward attendants but, practically, they were the active medical service of their wards. McKee tells a good yarn about an incident where Withers was forced to build his own jail and occupy it for an alleged infringement of discipline. It seems that Withers was told by a sergeant to carry a wounded soldier from a convoy ambulance to a distant tent because stretchers were being used for the badly wounded soldiers. When Withers noted that the human package weighed about twice his frail figure, he refused the distinctly impossible task. Court martial followed and Withers was ordered to jail. In fact, he was obliged to build his own jail which consisted of a tent with a barbed wire fence about it. His sympathetic companions among the soldiers destroyed the first jail erected and Withers was forced to build another. He did. The sentence was for one month and McKee insists that it was during the exposure in this miserable tent-jail that Withers contracted serious pulmonary symptoms for which he was later invalided home.

Sanford Withers was a hunter and fisherman. He owned two ranches in Colorado where he hunted deer. He was in the process of homesteading one of these ranches. He had a cabin on the Gunnison River with four miles of the best trout

water in the world. One recent experience while hunting in the fall of 1937 may have had a great influence upon his physical condition. It seems that he had shot a buck and while in the process of retrieving the animal, Withers was taken with a terrific pain in the chest and he was forced to lie down and rest. Fortunately another member of the hunting party discovered Withers almost dead from pain and exposure. The friend built a fire and after warming up the Doctor, carried him toward the camp. This formula of a new fire, rest, resuscitation, and carrying was repeated at least five times before the main camp was reached.

McKee relates one other circumstance that brings out both the character and characteristics of Withers, for Sanford was a thorough student who grasped essentials of any subject promptly and from thenceforth his imagination, inventiveness and originality played with the standard facts that the professor presented in class. Withers had a contempt for ignorance or half-knowledge of any subject. He had no sympathy for position, rank or theory unless he believed that the individual merited such distinction. While still a student in Washington University he was conditioned in chemistry because he refused to attend some classes and spurned the University laboratory courses whose elementary training he had long ago completed in the practical laboratory with Dr. Cross. Of course, when he took the required examination to erase the condition, he passed with flying colors.

Sanford Withers was always engaged in experimental work with both radium and roentgen irradiation. He had fitted up a laboratory in his garage with high voltage apparatus. Some of these experiments included attempts at tenderizing the cheaper cuts of beef and the caponizing of chickens. At one time he was employed by a large well-known cereal company to devise methods of irradiating breakfast foods to prevent and destroy the development of weevils in their products. Withers' experiences with the loss and rescue of radium are related in Dr. Robert B. Taft's recent book on "Radium Lost and Found," pages 33 and 34.

From the entrance of Withers into the field of radiation therapy, there is a record of his constant contribution to the theoretical and practical progress of radium therapy. Paralleling this was his inclusion of high voltage roentgen-ray methods to amplify the attack upon cancer. A cooperative Tumor Clinic at Denver can serve well as an enterprise of merit and distinction and this whole project was Withers' idea.

"Who's Who in American Medicine" in 1925 gave him credit for possessing "one of the most complete libraries on the physics, chemistry and therapeutics of radium in the United States." He had kept it up to date since, collecting several thousand books, pamphlets, reprints and other tracts on the subject. He contributed many articles on radium and roentgen therapy to medical journals, edited "The Radium Therapist" in Denver for a while, compiled "A Bibliography on Radium" and prepared two "Short Courses on Radium Therapy."

He was a member of the American Radium Society (President, 1931), the American Roentgen Ray Society, British Institute of Radiology, Radiological Society of North America, St. Louis Dermatological Society, American Medical Association, and the American Electro-Chemical Society. He was elected a Fellow of the American College of Physicians in 1932. Dr. Withers was also a member of the American Society for the Control of Cancer and served Colorado as State Chairman of this organization. He was a member and Chairman of the Committee on Cancer Education of the Colorado State Medical Society. His medical fraternity was Phi Rho Sigma. He had maintained membership in the Rouen Post of the American Legion in St. Louis. He was a Mason, holding membership in the Emulation Lodge of Denver.

Dr. Withers married Miss Matilda J. Bransbetter, of Wellsville, Missouri, in 1924. She survives with two children, Guy, aged nine, and Jane, aged eleven; two brothers, Major George A. Withers, U.S.A. retired, of Clay Center, Kansas, and Major Guy Withers, U.S.A., retired of Washington, and three sisters, Miss Avis Withers of Washington, Mrs. Robert H. Robinson, of Yonkers, and Mrs. James Clore, of Washington.

The incidents of Withers' career, with which the readers of this Journal are concerned, would appear to be his attachment to and interest in the American Radium Society of which he was President in 1931, just ten years after admission to membership. During this period he contributed to each annual program upon such subjects as the ovarian sterilization dose, cancer of the corpus uteri, lead therapy, and numerous others. The following bibliography was compiled from the *Quarterly Cumulative Index* of the years of Dr. Withers' active speciality practice.

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Edward H. Skinner

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. B. Peirce, University Hospital. Ann Arbor, Mich. Annual Meeting: Atlantic City, N. J., Sept. 20–23, 1938.

American College of Radiology
Secretary, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting, 1938: To be announced.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: San Francisco, Calif., June 13–17, 1938.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Pittsburgh, Pa., Nov. 27–Dec. 2, 1938.

Radiological Section, Baltimore City Medical Society
Secretary, Dr. Howard H. Ashbury, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Special meetings may be called by the Chairman.

Radiological Section, Los Angeles Co. Med. Soc.
Secretary, Dr. M. L. Pindell, 678 S. Ferris Ave., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. Harry Hauser, 3395 Scranton Rd. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Denver Radiological Club
Secretary, Dr. E. A. Schmidt, 4200 E. 9th Ave., Denver, Colo. Meets third Tuesday of each month.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida State Radiological Society
Secretary, Dr. Harold O. Brown, Tampa, Florida. Meetings held twice a year, May and November.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets twice annually: in November and at annual meeting of Medical Association of Georgia in the spring.

Illinois Radiological Society
Secretary, Dr. E. P. Halley, Decatur and Macon County Hospital, Decatur, Ill. Meetings held quarterly, time and place designated by president.

Indiana Roentgen Society
Secretary, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

Long Island Radiological Society
Secretary, Dr. S. G. Schenck, 115 Eastern Parkway, Brooklyn, N. Y. Meets at Kings County Med. Soc. Bldg. on fourth Thursday of each month from October to May, at 8:30 P.M.

Michigan Association of Roentgenologists
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

Minnesota Radiological Society
Secretary, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

New York Roentgen Society
Secretary, Dr. H. K. Taylor, 667 Madison Ave., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

Pacific Roentgen Club
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Annual Meeting, May 20-21, 1938, Traylor Hotel, Allentown, Pa.

Philadelphia Roentgen Ray Society
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St

Pittsburgh Roentgen Society
Secretary, Dr. H. N. Mawhinney, Mercy Hospital. Two fall and two spring meetings—time and place designated by the president.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Fran-

*Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

cisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina Medical Assn.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary Dr. G. D. Carlson, 3121 Bryan St., Dallas, Texas. Next regular meeting in San Antonio, Oct. 22, 1938.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich. Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section on Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson, Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

CLINICAL CONFERENCE OF MIDWESTERN RADIOLOGISTS

The second annual Clinical Conference of Midwestern Radiologists was held at Kansas City, Missouri, at the Muehlebach Hotel, on February 11 and 12, 1938. The meeting was well attended and the following interesting scientific program was presented:

Friday Morning, February 11

Clinical Significance of the Tuberculin Test. Herbert L. Mantz, M.D., Director Tuberculosis Clinics, Health Dept., Kansas City.

Roentgenological Manifestation of Childhood Tuberculosis. E. R. Deweese, M.D., Radiologist, St. Mary's Hospital. Discussion—Hubert Parker, M.D. Attending Physician, St. Mary's Hospital.

Clinical, Roentgenological and Pathological Findings in Secondary Lung Tumors. Charles E. Bell, M.D., Assistant Radiologist, Research Hospital. Discussion—Frederick C. Narr, M.D.

Correlation of the Clinical and Roentgen Kymographic Findings. Graham Asher, M.D., Associate in Medicine, University of Kansas, School of Medicine.

Clinical Differentiation of Coronary Disease and Upper Abdominal Pathology. Joseph E. Welker, M.D., Assistant Professor of Medicine, University of Kansas, School of Medicine.

Clinical Analysis of Sudden Death from Cardiac Disease. C. G. Leitch, M.D., Pathologist, St. Mary's Hospital. Discussion—Galen Tice, M.D., Radiologist, University of Kansas Hospitals.

Evolution of Radiation Therapy for Carcinoma of the Cervix. E. H. Skinner, M.D., Consulting Radiologist, Kansas City General Hospitals. Discussion—David S. Dann, M.D.

Friday Afternoon, February 11

Symposium on the Breast

Anatomy of the Breast. H. C. Tracy, M.D., Professor of Anatomy, University of Kansas, School of Medicine.

The Roentgen Examination of the Breast. Ira H. Lockwood, M.D., Radiologist,Research Hospital.

Pathology of the Breast. Frederick C. Narr, M.D., Pathologist, Research Hospital.

Benign Lesions of the Breast. James E. Stowers, M.D., Attending Surgeon, Research Hospital.

The Visualization and Diagnosis of Breast Lesions by Means of Contrast Roentgenograms. N. Frederick Hicken, M.D., Associate Professor of Surgery, University of Nebraska, College of Medicine, Omaha, Nebraska.

The Surgical Treatment of Carcinoma of the Breast. Claude J. Hunt. M.D., Attending Surgeon, Research Hospital.

The Value of Radiation Treatment of Carcinoma of the Breast. Lewis G. Allen, M.D., Professor of Clinical Roentgenology, University of Kansas, School of Medicine. Discussion—E. H. Skinner, M.D.

Saturday Morning, February 12

Correlation of Clinical, Encephalographic and Ventriculographic Findings. F. R. Teachenor, M.D., Associate Clinical Professor of Surgery, University of Kansas, School of Medicine. Discussion—Dalen Tice, M.D.

Clinical Analysis of Low Back Pain. Frank D. Dickson, M.D., Chief Orthopedist, St. Luke's Hospital. Discussion—C. Edgar Virden, M.D., Radiologist, St. Joseph Hospital.

Clinical and Roentgenological Data in Brucellosis (Undulant Fever). Fred E. Angle, M.D., Attending Physician, Bethany Hospital. Discussion—Lewis G. Allen, M.D.

The Problem of Acute Intestinal Obstruction. Thomas G. Orr, M.D., Professor of Surgery, University of Kansas, School of Medicine.

The Value of the X-Ray Examination in Acute Intestinal Obstruction. David S. Dann. M.D., Radiologist, Menorah Hospital. Discussion—L. W. Paul, M.D., Radiologist, St. Luke's Hospital.

Clinical and Roentgenological Features of Endocrine Lesions. W. M. Ketcham, M.D., Attending Physician, St. Joseph Hospital. Discussion—C. Edgar Virden, M.D.

Clinical and Roentgenological Findings in Trauma of the Genitourinary Tract. R. Lee Hoffman, M.D., Chief Urologist, Research Hospital. Discussion—Ira H. Lockwood, M.D.

Saturday Afternoon, February 12

Clinical and Radiological Features of Menorrhagia. T. J. Sims, Jr., M.D., Associate in Obstetrics and Gynecology, University of Kansas, School of Medicine.

Ovarian Influence in Cancer. Ferdinand C. Helwig, M.D., Associate Professor of Pathology, University of Kansas, School of Medicine. Discussion—Lewis G. Allen, M.D.

Neurogenic Factors in Functional Gastrointestinal Disturbances. P. T. Bohan, M.D., Professor of Medicine, University of Kansas, School of Medicine.

It was decided to hold the 1939 meeting in Detroit, Michigan.

TRIBUTE TO MARTYRS OF RADIOLOGY

On February 12, 1938, at the Röntgen Institute of the Krankenhaus St. Georg in Hamburg, acting under the instructions of Dr. B. R. Kirklin, President of the American Roentgen Ray Society, the Secretary, Dr. C. B. Peirce, laid a memorial wreath on the monument erected in the courtyard of that institution by the Deutsche Röntgen-Gesellschaft in memory of the martyrs to radiology. Those present included Dr. Hermann Holthusen, Mrs. Holthusen, Mrs. Peirce and Dr. Holthusen's staff. Dr. Peirce made the following presentation comment:

"Dr. Holthusen, it is a great honor for me to represent the American Roentgen Ray Society and its President, Dr. B. R. Kirklin, here today.

"The homage which the Deutsche Röntgen-Gesellschaft has paid to the martyrs in radiology throughout the world is appreciated by your American colleagues.

"That such a memorial, rich in its simplicity, should have been placed in the court of the institution within which the late Dr. Albers-Schönberg (long an honorary member of the American Roentgen Ray Society) labored so fruitfully, increases the bond between us.

"We lay this wreath here in the name of the American Roentgen Ray Society as a token of its appreciation, and in honor of the contributions to science and the welfare of humanity by the former colleagues whose names have been inscribed on this shaft."

AMERICAN RADIUM SOCIETY

The Twenty-third Annual Meeting of the American Radium Society will be held at San Francisco, California, at the Clift Hotel instead of the Mark Hopkins Hotel, as previously announced, on June 13 and 14, 1938. The Janeway Lecture will be given by Dr. Henry Schmitz of Chicago on "Historical Retrospect of Carcinoma of the Uterus."

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

THEORETICAL PRINCIPLES OF ROENTGEN THERAPY. Edited by Ernst A. Pohle, M.D., Ph.D., F.A.C.R., Professor of Radiology, Chairman, Department of Radiology and Physical Therapy, University of Wisconsin, Madison, Wisconsin. Foreword by W. Edward Chamberlain, B.S., M.D., F.A.C.R., Professor of Radiology in the Temple University School of Medicine, Philadelphia, Pa. Cloth. Price, $4.50. Pp. 271, with 132 illustrations. Philadelphia: Lea & Febiger, 1938.

Since the War several American authors have attempted to furnish the radiologists of this country with books on therapeutic radiology. Unfortunately, most of these attempts were only partly successful or complete failures, chiefly because they were written in haste, were not sufficiently complete, lacked the critical analysis which a book of this kind should have and sometimes showed ignorance of clinical medicine and pathology. In Europe several first-class books had appeared, one of the latest and one of the best being a two-volume work edited by Perussia and Pugno-Vanoni, published in Italy in 1934. Until the last few years, the preparation of a satisfactory textbook on therapeutic radiology would have been difficult because of the rapid changes taking place in this field of medicine. MacKee had written an excellent book on the use of roentgen rays and radium in the treatment of cutaneous and other superficial conditions, which until now remains the best book on the subject in the English language, if not in any language.

The present work, which is the first of two volumes issued independently, is the result of the collaboration of five authors (Newell, San Francisco, Pohle, Madison, Stenstrom, Minneapolis, Lauriston S. Taylor, Washington, Francis Carter Wood, New York) under the editorship of Professor Pohle. As the title indicates, it deals with the biological and physical principles underlying roentgen therapy. The subject of radium therapy is entirely omitted. The first chapter by Dr. K. W. Stenstrom deals with the physics of roentgen rays, the second chapter by Dr. R. R. Newell with apparatus for roentgen therapy, the third chapter by Dr. Lauriston S. Taylor and Professor Pohle with the measurement of dosage, the fourth chapter by Dr. Francis Carter Wood with radiobiology and radiopathology, and the fifth chapter by Dr. Lauriston S. Taylor with protection from roentgen rays. These authors, as well as the editor, are to be heartily congratulated on having produced, in a limited number of pages, a book which deals satisfactorily with the several subjects mentioned and which enables not only the radiologic specialist but others who might be interested in the subject to obtain sound opinions on questions about which there are still some controversy, as well as on other questions which have long since passed into the realm of established fact. If any one of these chapters can be singled out, it is that by Newell on apparatus for roentgen therapy. The only reason for singling it out, however, is because of its discussion of recent developments in apparatus, especially in apparatus designed to generate roentgen rays at high potentials, and the possible influence of such apparatus on the treatment of cancer.

A. U. DESJARDINS

ATLAS OF SKELETAL MATURATION. By T. Wingate Todd, M.D., Ch.B., Manc.; F.R.C.S., Eng., Henry Willson Payne Professor of Anatomy, Western Reserve University; Chairman, Brush Foundation; Director, Hamann Museum; Director, Developmental Health Inquiry of the Associated Foundations, with the collaboration of colleagues and assistants. Cloth. Price, $7.50. Pp. 201, with 75 illustrations. St. Louis: The C. V. Mosby Company, 1937.

This book is the result of very extensive roentgenologic study of the development and growth of bone. In the author's introduction, he states his definition of the term, maturation, and discusses variants of the maturation process, the natural and therapeutic control of maturation, its relation to skeletal maturity, general growth and size of the individual, etc. The impossibility of measuring maturation by dimensions is explained. Maturity status does

not correspond with stature, weight or age. He stresses the importance of the control of the processing of roentgenograms and the correct orientation of the central ray. In this introductory portion he describes the plan of the investigation and study by which his results were obtained.

Part I constitutes the remainder of the book, this volume being confined to the study of the hand. Standards are given which represent successive stages of maturity from three months after birth to the age of sixteen years in girls and nineteen years in boys. They begin at three months of age and continue at three-month intervals up to the age of one year and thereafter at intervals of six months. They represent the accumulated records of children of Cleveland, Ohio, from all grades of society, except the destitute, without regard to nationality of origin, type of family line, stature or weight.

The method of choosing a standard is described in detail. Each represents a different period of growth and a series is given for boys and for girls so that comparison between the two can be made. Each standard or observation consists of an illustrative roentgenogram with maturity determinators listed on the opposite page.

Todd defines maturity determinators as the successive changes in outline of the ends of the shafts and in contour of epiphyseal centers of ossification which mark the progress of skeletal maturation up to its final adult form. He regards the proximal ends of the metacarpal bones as the most important determinators in standards 1 to 10 inclusive, that is, from the age of three months up to three years and nine months, and for this reason it is most necessary to understand their morphological composition. Dates of appearance of ossification centers are not considered determinators. Todd states that like the growing ends of long bones, they are related to vitamin activity. The precise age at which each center appears is greatly influenced by constitutional encroachments and by health, and therefore their utilization may be very misleading. The real advantage of noting ossification dates is the information given by them on the availability of mineral supply of bone and preparation of cartilage for ossification.

The illustrations are excellent. The atlas requires careful reading and study to grasp fully the author's analysis of his vast material and his conclusions. To most roentgenologists his method of roentgenologic assessment of bone growth is a new, and perhaps, radical, departure from previous methods, However, the work of Todd is definitely a more accurate appraisal of bone growth than has hiterto been attempted. Through his untiring and painstaking efforts and skillful interpretation of the roentgenological examination of many children, he has furnished standards of bone growth which will greatly aid in clearing the confusion, prevalent today in this special field.

R. S. Bromer

Medical Writing: Some Notes on its Technic. By James H. Dempster, M.A., M.D., Editor, *Journal of the Michigan State Medical Society* and Lecturer on Medical Writing, College of Medicine, Wayne University, Detroit. Cloth. Price, $2.50. Pp. 168, with 11 illustrations. St. Paul: Bruce Publishing Co., 1937.

This book on Medical Writing is written by an author who has had several years' experience on the staff of daily newspapers and more than a dozen years as editor of medical journals. Realizing the trials and tribulations of editors of medical journals, one can readily appreciate the urge which he felt in publishing this monograph, even if it does no more, as he suggests in his introduction, than impress prospective medical writers with the seriousness with which editors look upon medical contributions, and with the various details incident to their publication.

There are chapters on the editorial function, the preparation of medical papers, illustrations, bibliography, the listing of references, the manuscript, type and proofs, the dictionary, Greek derivatives, the history of medical journalism and copyright regulations. Two appendices are attached, the first on recommended reading, the second containing a list of medical journals of the United States. Much sound advice is given.

The first chapter discusses editorial policy, book reviews, the editor's fitness for his work and contributions of most interest to readers. The chapter on the preparation of medical papers contains a subheading on diction in which a plea is made for simplicity of style, avoidance of tautologic expressions and cumbersome and pedantic phrases. Punctuation,

the use of the split infinitive, quotations, the use of capital letters and case histories are other sections of this chapter. In the last, the prospective author is asked to distinguish between the essential and the non-essential and is urged to avoid the telegraphic style and to devote as much care to the composition of a case history as is given to the body of the article.

The chapter on illustrations includes subjects which cannot fail to be of great assistance to writers in the preparation of their illustrations. Processes of reproduction are described, the deep-line etching, the half-tone process, etc. There is much practical advice on the labelling of illustrations, on preparation of graphs, black and white and outline drawings, shaded and tone drawings, photographs, and legends and on the proper method of submitting illustrations.

In the chapter on bibliography, a section describes where references may be obtained, their use, how to consult the literature on medical subjects, etc. The necessity for careful and correct listing of references is emphasized, and the several methods of listing used in various journals are given in detail.

A most valuable chapter is that on type and proofs. To most medical writers, it is fair to assume, proof reading is an unknown accomplishment. The chapters on the dictionary and on Greek derivatives are to the point. The lack of Greek in the pre-medical curriculum is now almost universal, and is a deplorable development. A list of Greek stems and prefixes is included.

The book is small but is printed with a legible type and is written in a readable and pleasing style. The reader may feel that he already knows much or all of what is written, but Dr. Dempster quotes Samuel Johnson in his introduction, "Men more frequently require to be reminded than informed." With the ever increasing number of medical publications, with young writers daily appearing in print and with many older ones still trying the souls of editors, there can be no doubt that this book has place on the shelves of those who write, or intend to write, on medical subjects. A few trivial lapses such as the inclusion of a paragraph on a general news section under the subheading, book reviews, in no way detract from the value of the book.

R. S. Bromer

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., M.S., 105 Rutledge Ave., Charleston, S. C.

ROENTGENOGRAPHY OF THE FEMORAL NECK

A TECHNIQUE TO OBTAIN TRUE LATERAL AND ANTEROPOSTERIOR VIEWS

By EMMETT A. DOOLEY, M.D., F.A.C.S., new york; CHAS. W. CALDWELL, JR., A.B., M.D., danville, kentucky, and GEORGE A. GLASS, A.B., M.D., carteret, new jersey

STUDY of trauma or disease of the neck of the femur is facilitated by roentgenography of the femoral neck in two planes at right angles to each other. A technique has been devised by which true anteroposterior and inferosuperior (lateral) images are obtained. All exposures are made with the patient supine on a horizontal table. Potter-Bucky technique is preferred.

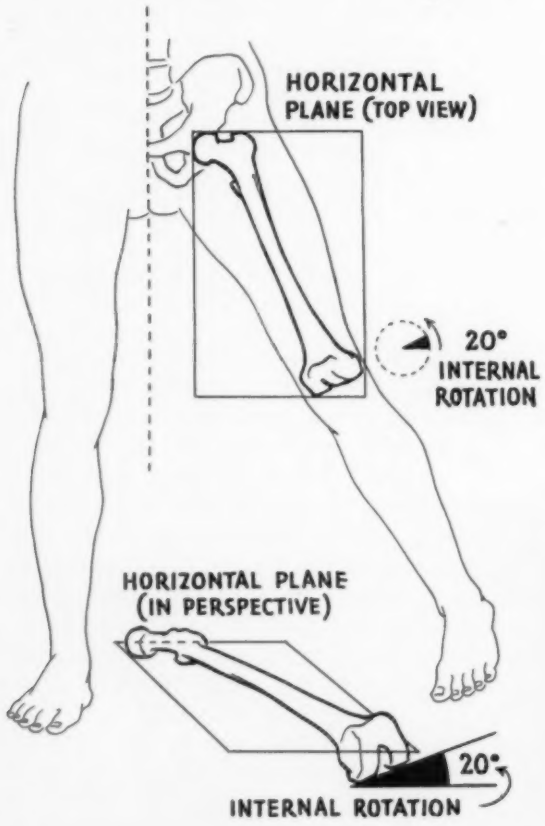

Fig. 1. Diagrammatic representation of femur in the anteroposterior view showing effect of internal rotation.

Technique for the Anteroposterior View.

1. The lower extremity is moderately abducted.

2. Grasp the thigh just above the knee, disregarding the position of the leg and foot entirely, and internally rotate the thigh approximately 20 degrees. The reason for this amount of internal rotation is that ordinarily the femoral neck is parallel to the film when the lower extremity is in this position (Fig. 1).

3. An exposure is then made with the tube centered over the femoral neck. The film should include at least 6 inches of the shaft for the calculation of the shaft-neck angle.

Fig. 2. True anteroposterior roentgenogram. Note position of lesser trochanter.

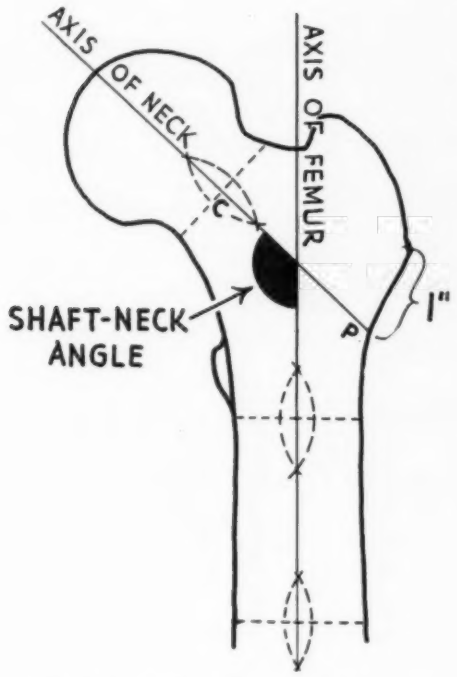

Fig. 3. Tracing from anteroposterior roentgenogram showing calculation of the shaft-neck angle.

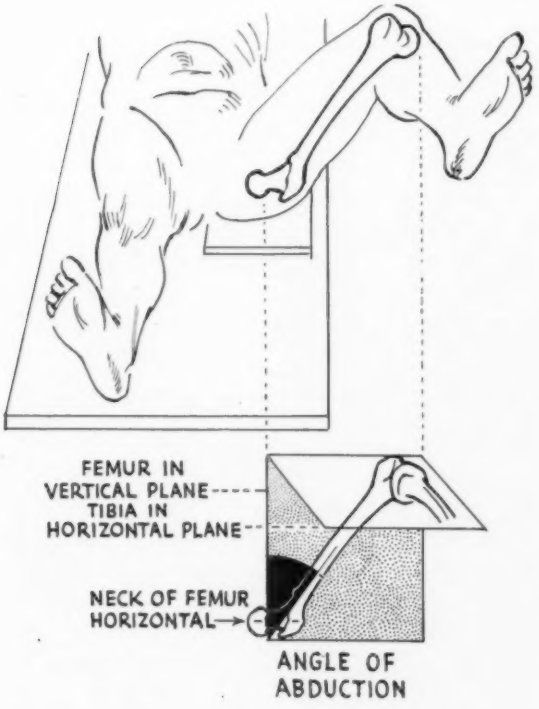

Fig. 4. Diagrammatic representation of femur in position for lateral roentgenogram, showing effect on neck of femur.

Fig. 5. True lateral roentgenogram.

A rough check, roentgenographically, for the desired position is that the lesser trochanter be nearly obscured by the shaft (Fig. 2).

Technique for the Lateral View.

From a tracing of the anteroposterior

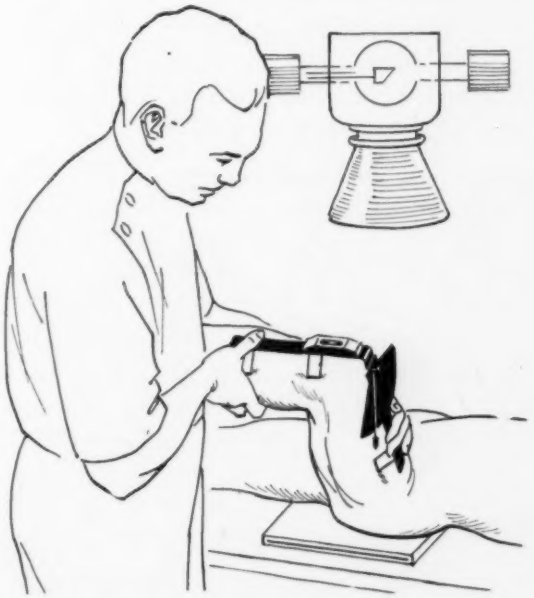

Fig. 6. Caldwell-Glass inclinometer. The instrument consists of a metal right angle, each arm approximately 10 inches long; fixed to one arm is a small spirit level and to the other a plumb line protractor. Flanges at the angle and extremities assure exact application.

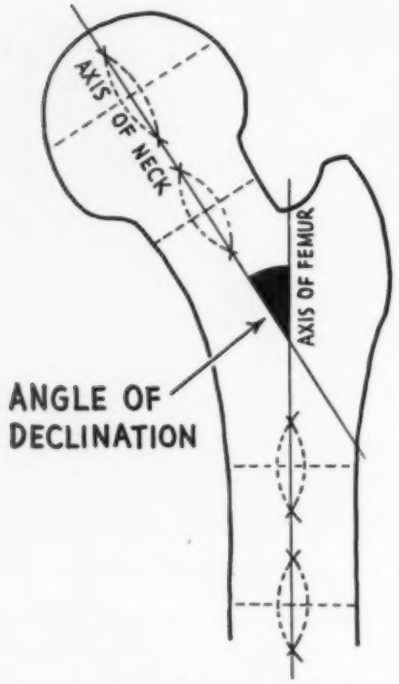

FIG. 7. Tracing from lateral roentgenogram showing calculation of angle of declination.

roentgenogram, the shaft-neck angle is determined in the following manner:

1. Bisect the femoral shaft.

2. A point, *P*, is marked off with a compass 1 inch below the most prominent part of the greater trochanter.

3. A point, *C*, is found which bisects the middle of the femoral neck.

4. A line, *CP*, is then drawn connecting the two points. Where it crosses the axis of the shaft it forms the shaft-neck angle (Fig. 3). With a little experience this angle can be adequately determined with a transparent protractor on the wet plate.

Then, with the patient supine—

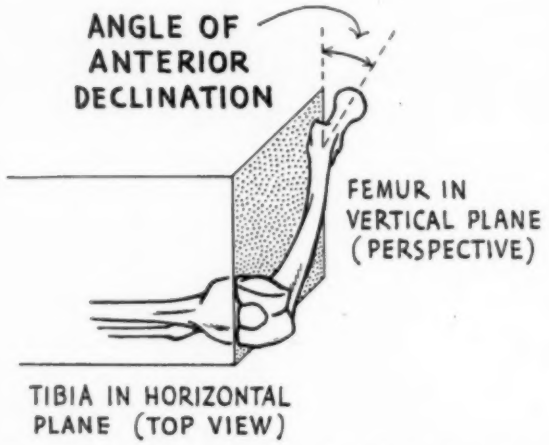

FIG. 8. Schematic representation illustrating why the projection of the femoral shaft may be used as a base line from which to measure the anterior declination of the femoral neck.

1. Flex the hip and knee to 90 degrees in the sagittal plane.

2. Abduct the thigh the difference in degrees between the shaft-neck angle and 90 degrees (shaft-neck angle $130°-90°=40°$, therefore abduct 40°). At this point the tibia must be kept horizontal and the

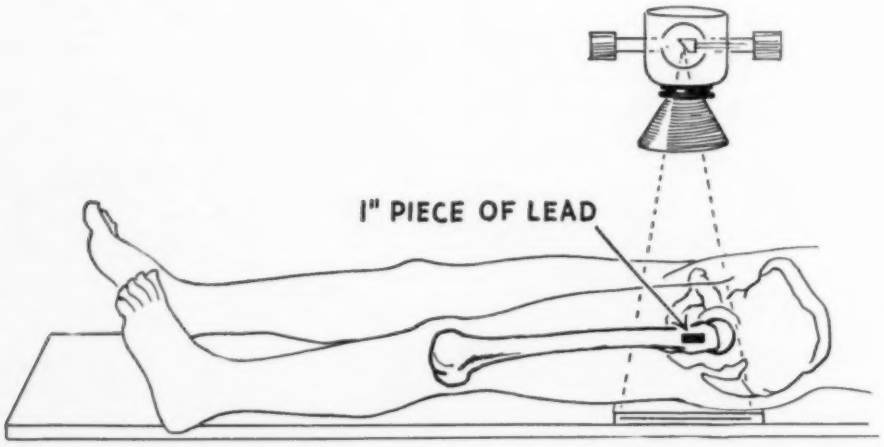

FIG. 9. The position of the 1 inch piece of lead in relation to the greater trochanter and cassette.

hip and knee at right angles. In this position the neck of the femur is horizontal or parallel to the film (Fig. 4). An exposure is then made with the tube centered over the femoral neck (Fig. 5).

An inclinometer (Fig. 6) has been devised (C.W.C., G.A.G.) which assists in:

1. Holding the knee at a right angle.
2. Holding the leg horizontal.
3. Measuring the deviation of the shaft from the vertical.

Comment. At first glance such an exacting technique may seem unnecessary, but from these images the shaft-neck angle and the angle of anterior declination of the femoral neck can be accurately measured. The measurement of the shaft-neck angle has been described above. The angle of anterior declination is measured from a tracing of the lateral roentgenogram (Fig. 7), and represents the deviation of the femoral neck from the plane of the posterior surface of the femoral condyles. When the tibia is held horizontal and the knee at a right angle, the superior articular surface of the tibia lies in a perpendicular plane which parallels the posterior surface of the femoral condyles and the axis of the femoral shaft. Then, the projection of the femoral shaft in the roentgenogram may be used as a base line from which to measure the anterior declination of the neck (Fig. 8).

When accurate linear measurement of the neck is desired, a piece of lead, exactly 1 inch long, incorporated in a strip of adhesive, is fixed to the skin at the level of the greater trochanter, so that its long axis parallels the cassette at the time of the anteroposterior exposure (Fig. 9). The magnification of the 1 inch lead can be transferred by proportion to the femoral neck (Fig. 10).

Fig. 10. Determination of actual length of femoral neck.

SUMMARY

1. A technique for obtaining true roentgenograms of the femoral neck in two planes is described.

2. An instrument (inclinometer) for placing the femoral shaft at any predetermined angle with the vertical is presented.

3. Methods of accurate mensuration of the femoral neck are outlined.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Travers, J. Townsend. Roentgenologic findings of post-traumatic sequelae of head injuries; an encephalographic study. *Radiology*, June, 1937, *28*, 704–713.

A review of the literature concerning post-traumatic sequelae from brain injuries is given. The author reports 14 cases of his own. He found that the cases should be studied by means of an encephalogram or ventriculogram. Symmetrical filling of the ventricle and subarachnoid spaces or dilatation of one or both ventricles without ventricular shift, definitely rules out a subdural hematoma. When a subdural hematoma was present there was a ventricular shift away from the side of the lesion, while in the presence of scar tissue resulting from a laceration of the brain there may be a ventricular shift toward the lesion. The differential diagnosis between these two lesions is important, because early surgery is indicated when a hematoma is present. The study of these cases having post-traumatic symptoms by means of air injections is not harmful and many cases of traumatic headaches with no demonstrable pathology have been markedly improved following encephalography.—*J. H. Harris.*

Jupe, M. H. Ventriculography. *Brit. J. Radiol.*, March, 1936, *9*, 147–160.

With the detailed presentation of 15 cases of special interest and illustrative points, the author outlines the main considerations for air injection. All methods, particularly encephalography, are dangerous in cases exhibiting clinical evidence of marked rise in intracranial pressure. Encephalography is absolutely contraindicated when there is the possibility of a posterior fossa lesion. Ventriculography is not attended with the immediate disturbance which accompanies encephalography.—*W. R. Brooksher.*

Shebesta, E. M. Gangrene of face produced by lymphosarcoma. *Radiology*, July, 1937, *29*, 33–36.

A case of lymphosarcoma is reported which was not diagnosed correctly until autopsy. The origin of disease was the left maxillary sinus and in the later stages led to a gangrene of the face. The lymph nodes were not involved until late in the disease.—*J. H. Harris.*

NECK AND CHEST

Sowers, B. F. Mastitis following the use of thorium dioxide: report of case. *Proc. Staff Meet., Mayo Clin.*, August 25, 1937, *12*, 529–531.

Report is made of the occurrence of mastitis, necessitating simple mastectomy, in a breast into which thorium dioxide had been injected as a diagnostic procedure twenty-two days previously. Roentgenograms of the thorax revealed radiopaque material, shown by detailed studies to be within the ducts. It is suggested that the contrast medium, in this case, may have been diffused throughout the mammary tissue.—*W. R. Brooksher.*

Moschcowitz, Eli. Superior sulcus tumor. *J. Mt. Sinai Hosp.*, Jan.-Feb., 1937, *3*, 198–200.

A full case report is presented. The main features of the disease are: (1) pain around the shoulder and upper arm; (2) occasional loss of power and atrophy of the muscles of the hand; (3) an invariable Horner's syndrome; (4) a circumscribed roentgenographic shadow at the apex of the lung with destruction of the posterior portions of the 1st, 2nd and 3rd ribs and often of the adjacent vertebrae. It is felt that this is not a new disease entity but rather a syndrome provoked by a lesion of varying character and origin invading the region of the superior sulcus. These squamous cell tumors are in most instances carcinomata arising from the terminal bronchi of the lung. Such tumors always occur at the periphery of the lung and are by no means strictly localized to the superior pulmonary sulcus. Owing to their peripheral character, invasion of the bony chest wall is exceedingly common, giving rise to radiation pain. Furthermore, these tumors are always sharply circumscribed from the lung parenchyma.—*W. R. Brooksher.*

FROST, THOMAS T., and WOLPAW, SIDNEY E. Intrathoracic sympathoblastoma producing the symptomatology of a superior pulmonary sulcus tumor (Pancoast). *Am. J. Cancer*, March, 1936, *26*, 483–492.

Studies were made both ante and post mortem of a case which presented the four cardinal clinical findings which Pancoast in 1932 laid down for superior pulmonary sulcus tumors:

A. Pain about the shoulder, axilla, or inner side of the arm.

B. Horner's syndrome.

C. Loss of power and the wasting of the muscles of the hand.

D. Roentgen evidence of a small homogeneous shadow at the apex of the lung, with destruction of the posterior parts of one or more ribs and often of the adjacent vertebrae.

The authors present their findings in detail and discuss the differential diagnosis, chiefly of the histology, at some length, arriving quite logically at a diagnosis of sympathoblastoma. In the literature they found that at least 6 other tumors which fulfilled Pancoast's criteria for superior pulmonary sulcus tumors were found at autopsy to be of bronchogenic origin. Therefore they concur with Weller, Fried, Browder and De Verre in concluding that a clinical syndrome which has been described under the name of superior pulmonary sulcus cannot be attributed to a specific pathological entity.—*J. S. Weber.*

MENNE, FRANK R., and BIRGE, RICHARD F. Primary leiomyosarcoma of the upper third of the esophagus. *Am. J. Digest. Dis. & Nutrition*, Jan., 1937, *3*, 848–851.

Detailed report is made of a patient with this rare tumor, presenting an associated abscess formation with sinus in the neck. Roentgen diagnostic study is presented. High voltage irradiation did not prove of value. Death resulted from hemorrhage with asphyxia due to aspiration of blood.—*W. R. Brooksher.*

BABEY, A. Displacement of the esophagus by cardiac lesions other than mitral stenosis. *Am. Heart J.*, Feb., 1937, *13*, 228–237.

The observations pertain to alteration in the position of the barium-filled esophagus as observed in the first or right oblique position. The five important structures which may impinge on the esophagus are, from above downward: the aortic arch, the pulmonary artery, the left auricle, the left ventricle, the descending aorta. Displacement of the esophagus is most frequently due to the enlargement of the left auricle associated with mitral stenosis. Congenital heart disease rarely displaces the esophagus, however cases of coarctation of the aorta, patent ductus adhesions, and interatrial septal defect are described in which significant displacement was present. Slight displacement was seen in one case due to enlargement of the left auricle associated with aortic stenosis. Occasionally there is displacement in aortic insufficiency without other valve lesion. Likewise cardiac hypertrophy associated with hypertension, auricular fibrillation, thyrotoxicosis, and complete heart block may produce a slight distortion of the contour of the esophagus. In such instances the enlargement of the left auricle is but a part of the generalized cardiac enlargement. A case of aneurysm of the heart causing pressure on the lower end of the esophagus is mentioned. Thus the author believes that the configuration of the esophagus cannot be considered as pathognomonic of any one type of cardiac lesion and that other evidence must be considered in reaching a correct diagnosis.—*W. A. Evans, Jr.*

GOLDEN, J. S., and BRAMS, W. A. Extreme cardiac enlargement. *Am. Heart J.*, Feb., 1937, *13*, 207–216.

The authors have collected from the literature 38 cases where the weight of the heart exceeded 1,000 gm. and added 9 cases of their own. The largest heart on record is said to have weighed 5 pounds but nothing else is known of the heart nor of the disease from which the patient suffered. Pericardial adhesions and deformity of the aortic valve were the conditions most commonly associated with extreme enlargement. There was a great predominance of males in the series. In 2 of the cases the heart disease was associated with kidney disease and hyptertension. In one instance of extreme enlargement (1,475 gm.) no clinical or anatomical basis for the cardiac hypertrophy could be ascertained.—*W. A. Evans, Jr.*

KEMP, J. E., and COCHEMS, K. D. Studies in cardiovascularsy philis. Teleoroentgenography in the diagnosis of early syphilitic aortitis. A comparison of the findings in 1,000 syphilitic and 600 nonsyphilitic individuals. *Am. Heart J.*, March, 1937, *13*, 297–307.

The authors point out the importance of distinguishing aortitis from the changes produced

by hypertension and arteriosclerosis before the serious complications of aortic insufficiency and saccular aneurysm have developed. There is a great discrepancy between the clinical and autopsy diagnosis of early syphilitic aortic disease. The authors base their study on 1,600 satisfactory teleroentgenographic examinations and the accompanying records from the Syphilis Division of the Public Health Institute in Chicago. There was about the same incidence of cardiovascular abnormality (30 per cent) in the syphilitic and non-syphilitic groups. There was progressive increase in the average width of the aortic arch with advancing years in the patients without cardiovascular disease which was of equal degree in both the syphilitic and non-syphilitic groups. In the non-syphilitic patients without heart disease there was borderline or definite dilatation of the aortic arch (over 6.7 cm. in males or 6.2 cm. in females) in 7.4 per cent of the patients, while approximately the same incidence (7.9 per cent) was present in the corresponding syphilitic group. Of the patients having a diagnosis of syphilitic aortitis 22.5 per cent had no teleroentgenographic evidence of aortic widening and unquestionable aortic dilatation was present in only 59.7 per cent of the group. The authors conclude that the diagnosis of uncomplicated syphilitic aortitis cannot be made by teleroentgenography alone and that fluoroscopy and clinical evaluation of the signs and symptoms are essential.—*W. A. Evans, Jr.*

Gitlow, Samuel. Coarctation of the aorta, with report of a living case. *New York State J. Med.*, Jan. 15, 1937, *37*, 155–158.

Following a complete discussion of the lesion, report is made of a case of coarctation of the aorta in a patient now under observation since 1926.—*W. R. Brooksher.*

Hennell, Herman. Acquired giant air cysts of the lung, with special reference to their pathogenesis and pneumodynamics. *J. Mt. Sinai Hosp.*, Nov.-Dec., 1936, *3*, 155–161.

Report is made of a case of acquired air cysts in the lung in a patient with a history of asthmatic bronchitis associated with suppurative sinusitis extending over a period of seventeen years. The initial roentgen studies suggested air cysts but in the differentiation from localized pneumothorax, bronchographic examinations with iodized oil and artificial pneumothorax were employed as additional aids. Subsequently, iodized oil was introduced into the upper cysts, this procedure outlining the lower cysts as well. The cysts were determined to be firmly adherent to the anterior chest wall, thus preventing their rupture and precluding further and excessive enlargement. The intracystic pressures were studied with the aid of a water manometer and it was discovered that the intracystic pressure was markedly positive and that it varied greatly during inspiration and expiration. The size, growth and dymanics of an air cyst are determined largely by the character of its bronchial communication; when this communication is free, allowing ingress and egress of air during inspiration and expiration respectively, the air cyst will remain of small size or enlarge very slowly. When the bronchial communication is in the nature of a check-valve, allowing air to enter the cyst during inspiration, but preventing its egress during expiration, the cyst will tend to enlarge and will quickly reach "giant" proportions. The other two influences which oppose undue enlargement of giant air cysts are: (1) pleural adhesions and (2) the elastic resistance of the functioning pulmonary parenchyma. As a result of the iodized oil injection in this individual, an exudative reaction developed, which led to the obliteration of the bronchial communication and the cysts have shown a marked tendency to decrease by absorption.—*W. R. Brooksher.*

Peirce, Carleton B., and Dirkse, Paul R. Pulmonary pneumatocele (localized alveolar or lobular ectasia); certain considerations in cystic disease of the lung. *Radiology*, June, 1937, *28*, 651–667.

The authors take exception to the common practice of labeling all cystic disease of the lung as congenital in origin. This exception is based upon the fact that there are few if any reports of changes in the lungs of newborn infants or very young children at autopsy warranting the diagnosis of congenital cystic disease.

They elect to classify cystic pulmonary disease as:

I True congenital pulmonary cyst or cysts;
II (a) Chronic interstitial pneumonitis with emphysema;
(b) Chronic bullous emphysema;
III Cystic bronchiectasis;
IV Pulmonary pneumatocele (localized alveolar or lobular ectasia).

The majority of cases reported fall in groups III and IV. Cystic areas are likely to develop in association with bronchopneumonia as a result of (*a*) bronchiectasis due to the damage to the bronchial and bronchiolar walls or (*b*) from focal acute lobular vesicular emphysema which may not be relieved because of incomplete resolution in or repair of proximal airway, or (*c*) from peripheral bullous (subpleural) emphysema by means of the rupture of the bronchial walls which permit an escape of air into the interstices.

The cases of pulmonary pneumatocele include those which present a single or a few contiguous grossly emphysematous alveoli. The authors believe the origin of the pneumatocele is due to acute lobular emphysema associated with lobular pneumonia. A persistent check valve obstruction of the bronchial lumen being due to either non-resolution of the initial inflammation of the bronchus or subsequent distortion by the dilated air spaces.

A number of reproductions of roentgenograms showing examples of the different groups are given.—*J. H. Harris.*

FLEISCHNER, F. Zur Röntgenologie der plattenförmigen Atelektaseherde. (Roentgenology of the horizontal linear areas of pulmonary atelectasis.) *Röntgenpraxis*, June, 1937, *9*, 381–384.

In previous communications the author demonstrated that the peculiar horizontal linear shadows seen mostly in the lower lung fields represent foci of resorption atelectasis. Their cause and horizontal distribution is due to a peculiar mechanism. Due to the fact that the lungs are enclosed in the rigid frame of the thoracic cage, tissue particles which become atelectatic by a bronchial plug are unable to contract concentrically. The parenchyma is stretched between the thoracic wall and the plugged bronchus in the neighborhood of the hilum, but cannot well contract in this direction because the lung is unable to tear itself loose from the thoracic wall. However, collapse is usually possible at right angles (most often in the craniocaudal direction), because the neighboring air-containing lung particles are able, through a longitudinal stretching, to fill in the space left free by the atelectatic collapse. In addition, the diaphragm moves upward and with the additional impairment of the respiratory movement, it likewise replaces some of the lost space.

If the area of horizontal atelectasis extends to the interlobar septum, the direction of the force of the atelectatic pull becomes indirectly visualized by the changed direction of the interlobar septum, which becomes angulated toward the atelectatic area.

Several illustrations show the horizontal atelectatic areas throughout the bases, and the kinked and displaced interlobar septa.—*Eugene Freedman.*

DICKY, LLOYD B. Coincident pulmonary tuberculosis and bronchiectasis in children. *Am. J. Dis. Child.*, April, 1937, *53*, 1047–1052.

The differential diagnosis between pulmonary tuberculosis and bronchiectasis is a frequent problem when dealing with adult patients. Basilar lesions of a chronic infectious nature are seen less frequently in children but often enough so that the determination of their nature is important. That tuberculosis may be a cause of localized bronchiectasis through changes in the bronchi by prolonged tuberculous ulceration has, of course, been recognized for a long time. In proof of the fact that the two conditions may occasionally occur in the same child and probably independent of each other, Dickey reports 2 cases.

The features common to the histories of both patients were: (1) exposure to tuberculosis during childhood; (2) a diagnosis of the childhood type of tuberculosis at an early age; (3) a history and findings of bronchiectasis, proved in each instance by the injection of iodized poppyseed oil and the taking of roentgenograms. At the approach of adolescence, in each girl there was a lesion of the base of the left lung, with the production of considerable sputum which was found to contain acid-fast bacilli only after concentration but which usually showed them then. When bronchiectasis and tuberculosis occur together, acid-fast bacilli occur in the sputum considerably diluted by material from bronchiectatic cavities, and finding them offers difficulties similar to those encountered in searching for them in pleural fluid or fluid from the spinal canal. Negative results of examinations of sputum do not rule out tuberculosis of the lower lobes.—*R. S. Bromer.*

CLERF, LOUIS H. Carcinoma of the bronchus. *Radiology*, April, 1937, *28*, 438–444.

In order that early diagnosis of carcinoma of the bronchus may be made the clinician should

consider the possibility of such a condition when the symptoms are cough, with or without sputum, blood streaking, pain and wheeze. Unexplained cough, hemoptysis and wheeze also warrant bronchoscopy. Iodized oil instillation should be employed as a supplementary measure.—*J. H. Harris.*

Rosendale, Raymond S., and McKay, Donald R. A study of 57 cases of bronchogenic carcinoma. *Am. J. Cancer*, March, 1936, *26*, 493–506.

A study is made of 57 cases of bronchogenic carcinoma observed at the Buffalo City Hospital from 1924 to 1934. Bronchogenic carcinoma and uterine carcinoma each constituted 7.5 per cent of the malignancies found at autopsy during the period of 1925 to 1934. However, the authors doubt that this is a true percentage of relative incidence. Ninety-one per cent of the 57 cases were males and 75.4 per cent had been exposed to irritating atmospheric factors in their occupations. Four forms of bronchogenic carcinoma were recognized grossly but the most frequent was a unilateral massive hilar nodule. The histology, metastases and clinical findings are discussed. The diagnosis was missed in 50 per cent of the roentgen examinations made on 30 patients later examined at autopsy. The error in most of these was due to secondary pulmonary or pleural pathology which obscured the tumor. The authors conclude "that bronchogenic carcinoma occurs frequently enough for it to enter the differential diagnosis of all obscure chest diseases in individuals over thirty years of age."—*J. S. Weber.*

ABDOMEN

Stein, Irving F. Why pneumoperitoneum? *Radiology*, April, 1937, *28*, 391–398.

The correct diagnosis of confining pelvic conditions can be made by pneumoperitoneum according to the technique used by the author. CO_2 is instilled into the abdominal cavity either through the uterus and tubes or through the abdominal wall. The patient is then placed in a partial knee-chest position and films are taken. No bad results have been experienced in over 800 cases. The uterus and ovaries are clearly outlined by the method and any variation from normal can be detected.—*J. H. Harris.*

Beutel, A. Pleura-Magenfistel. (Fistula between pleura and stomach.) *Röntgenpraxis*, Feb., 1937, *9*, 111–115.

The fistulous tracts between the stomach and pleural cavity are usually caused by a perforation of a gastric ulcer or cancer, by an incarceration of a hiatus hernia of the stomach with secondary gangrene, by a traumatic rupture of both organs, and finally by suppurative processes of the abdominal or the pleural cavity. In most of the instances the communication occurs between the left pleural cavity and the stomach, but very rarely the fistula may extend into the right pleural cavity.

The rôle of the roentgen examination is to establish the extent and ramification of the fistulous tract, the organs involved by it, and if possible to determine whether the disease of the stomach or pleura is the primary site.

The author reports the case of a patient, aged thirty-eight, who in 1930 attempted to commit suicide. The bullet was removed from the left pleural cavity and empyema ensued, which had to be drained on several occasions. In 1936 the patient was readmitted on account of marked loss of weight, of attacks of nonproductive, severe cough, and a remaining fistulous opening at the level of the eleventh rib. Iodipin was injected into the fistulous opening. Several pockets of the empyema cavity became visualized. In addition, an extensively ramified fistulous tract was seen under the diaphragm, and finally the contrast material was found to extend into the stomach. The roentgen diagnosis of chronic empyema with rupture into the left abdominal cavity and into the stomach was made. These findings were confirmed at subsequent autopsy.—*Eugene Freedman.*

Kelly, James F., and Dowell, D. H. The value of the preliminary film without opaque media in the diagnosis of abdominal conditions. *Radiology*, July, 1937, *29*, 104–110.

Stress is placed upon the importance of a survey film examination of the abdomen preliminary to all roentgen studies of the abdominal viscera. This is necessary as important pathology may be obscured by the opaque material used in the study. The authors recommend a film of the abdomen preliminary to all laparotomies when the least doubt exists regarding the diagnosis.—*J. H. Harris.*

GORDON, ARNOLD M. Syphilis vs. carcinoma of the stomach: thorium dioxide injection. *J. Iowa Med. Soc.*, Dec., 1936, *26*, 674–676.

Detailed presentation is made of a case in which the diagnostic problem was to determine whether malignancy or syphilis was the factor in a stomach, the roentgenological appearance of which suggested carcinona. The serology was positive. Thorium dioxide injection showed that the liver was free of malignant disease, enhancing the possibility that the gastric lesion was syphilitic in origin. The diagnosis was so confirmed.—*W. R. Brooksher.*

MINNES, JAMES F., and GESCHICKTER, CHARLES F. Some clinical features of carcinoma of the stomach. *Am. J. Cancer*, August, 1936, *27*, 740–748.

An analysis of 541 cases of carcinoma of the stomach are presented, and 370 cases of the series, which were followed to death or for five years, revealed only 3.5 per cent five-year cures. Clinical observations, pathology, diagnosis and treatment of the series (no mention is made of radiation treatment) are discussed. In spite of the general belief that competent roentgen examination is conclusive, the authors found that in 197 cases where the roentgen examinations were adequately reported, negative reports were made on 34 cases, later proved to have carcinoma of the stomach. The greater portion of the negative reports, however, were made prior to 1915.—*J. S. Weber.*

BERG, H. H. Fortschritte auf dem Gebiete das Verdauungskanals. (Klinische Röntgenuntersuchung des akuten Bauchfalls.) (Developments in the field of the gastrointestinal tract. (Clinical roentgen examination of the acute abdomen).) *Röntgenpraxis*, April, 1937, *9*, 217–229.

The indications for roentgen examination have changed during the past years. While a decade ago the roentgen examination was more or less utilized only to confirm the carefully established clinical diagnosis, at present the roentgen examination is carried out at first whenever it is necessary to diagnose a condition rapidly and with clarity. However the plan, the choice of type of procedure and the intelligent coördination of the diagnostic, clinical and roentgenological examinations is important, and one must consider the economy of the various diagnostic procedures as well as the realization of their limitations and possible sources of error.

The author discusses the technique and plan in examination of the acute abdomen in connection with illustrative cases. A large group comprises those acute cases which are admitted with the clinical symptoms of colicky pain, abdominal shock, intestinal obstruction, or perforation. In these cases the diagnosis has great bearing on the selection of the best method of treatment. One has to consider the conditions which may produce similar clinical symptoms, like tubal pregnancy, nephrolithiasis, perinephritic abscess, diseases of the circulatory apparatus (coronary disease, angina, aneurysm, thrombosis or embolus of the mesenteric blood vessels), basal pneumonia, spontaneous pneumothorax, and incarcerated hernias of the gastrointestinal canal. In these cases, author carries out the following plan: (1) clinical examination; (2) examination of the blood microscopically and chemically; (3) examination of urine; (4) examination of stool or vomitus. This is followed according to the clinical findings by (*a*) roentgen study of the thorax, or (*b*) of the abdomen. Flat plates of the abdomen are taken with horizontal and vertical rays, and search is made for fluid levels, free air, or concrement formation. Occasionally the colon and the stomach are examined with contrast material and with great care, but only in cases where the contrast material is contemplated to be surgically removed immediately afterward.

Perforation of a duodenal or gastric ulcer is diagnosed by the presence of free air in the abdomen. Necrosis of the pancreas, this dramatic disease of an autodigestive process, occurs in the majority of cases as a complication of gallbladder disease. This diagnosis can be confirmed by the finding of air distention of the stomach and a marked dilatation of the second portion of the duodenum with thickened rugae associated with compression in the region of the duodenojejunal junction as seen after the administration of a slight amount of contrast material. The transverse colon is likewise distended by air. Frequently, there is a beginning basal pneumonia or pleurisy due to transgression of the inflammation into the pleural cavity. These findings are typical. Not infrequently, pancreatic necrosis is associated with abscess formation, perforation and fistulous tract formation or production of retention cysts. These changes are occasionally indicated by round

pressure defects on the greater curvature side of the stomach or on the midportion of the transverse colon.

Signs of transgression of abdominal infection into the thoracic cavity (the so-called pleuropulmonic syndrome) are found in addition to pancreatic necrosis in cases of abscesses of the liver and gallbladder. Author demonstrates 3 cases where in addition to this syndrome the air-containing bile ducts became visualized. This occurs when the gallbladder perforates into the duodenum or colon, or a duodenal ulcer into the common duct, and in cases where gas-forming microorganisms are present in the bile ducts. Cholangitic abscesses may become similarly visualized by air.

The diagnosis of ileus can be established with the aid of flat films with the rays in a horizontal direction. One has to keep in mind that in cases of mesenteric vein thrombosis, with infarction of an intestinal segment, the roentgenogram may reveal ileus-like changes.

The differentiation between a gallbladder tumor and a peri-appendiceal abscess can be established by the utilization of contrast materials (barium enema as well as oral barium), which will demonstrate pressure defects either on the cecum or descending duodenum.

Appendicitis-like attacks on the left side are commonly caused by diverticula of the sigmoid. This condition can be easily diagnosed with the aid of the barium enema.

To determine the source of bleeding from the gastrointestinal tract one has to employ the relief study of the mucosa after the administration of small amounts of contrast material. Esophageal varices can be diagnosed with a swallow of barium. After a gastric hemorrhage one should wait fourteen days before roentgen examination is to be carried out unless immediate surgery is indicated, in which case the patient may be examined in the recumbent position without palpation. The author was able to diagnose once an arterial stump measuring about 4 mm. in diameter in the center of an ulcer crater, which was visualized as an irregular prominence extending into the crater. This was confirmed by a subsequent autopsy.—*Eugene Freedman.*

Hansen, K., and Simonsen, M. Röntgenologische Beobachtung und Darstellung der allergischen Gastritis und des allergischen Pylorospasmus. (Roentgenologic observation and visualization of allergic gastritis and allergic pylorospasm.) *Röntgenpraxis*, March, 1937, *9*, 145–151.

Allergic reactions are elicited after the reinjection or reabsorption of a foreign substance to which the organism is already sensitized (antigen). The allergic phenomena are generalized, yet certain organs may show an excessive response to the stimulus. Nutritive allergy is elicited by food materials. The antigens are various fruits and vegetables, flour, fish, egg white or yolk, cow's milk. In adults the allergic gastrointestinal reactions are more frequent than surmised and the symptoms consist of pressure and pain in the gastric region, associated with nausea and vomiting.

The author describes 2 cases where after the neutral barium meal the gastric rugae were normal, but on re-examination, after an egg yolk or milk containing barium meal, the gastric rugae were found widened, indicating a "hyperergic" gastritis. In addition, a pylorospasm occurred in both cases.—*Eugene Freedman.*

Arens, Robert A., and Mesirow, Sidney D. Gastric mucosal relief; a modified sedimentation method, using a colloidally suspended barium sulphate. *Radiology*, July, 1937, *29*, 1–11.

A preliminary report is made of the authors' experience with a modified sedimentation method of examining the gastric mucosa. The patient is given a mixture of "Rugar" diluted 1 to 15 with water and is placed on his right and left side and abdomen for fifteen minutes. Then he is given seidlitz powders and immediately films are taken. This special examination is followed by the usual fluoroscopic examination. It is felt that this method has some advantages in the occasional case.—*J. H. Harris.*

von Pannewitz, G. Zur Röntgendiagnostik des Dünndarms. (Roentgen diagnosis of small intestinal lesions.) *Röntgenpraxis*, Jan., 1937, *9*, 11–25.

The visualization and observation of the small intestines is difficult and time-consuming, consequently this part of the intestinal tract is neglected by roentgenologists. The shape, position and contraction of the small intestines is variable and the only constant finding in this part of the intestinal tract is the inconsistency. For this reason, findings should not be reported

as pathological unless they are found unchanged during several observations. Pansdorf's method, consisting of the administration of one swallow of barium at 15-minute intervals, and fluoroscopic study or roentgenograms at one-half hour intervals, allows the complete visualization of the small intestinal tract.

Extra-enteral tumors are recognized by the displacement of certain loops, producing an arch-like displacement of the intestinal segment. It is important to observe the mucosal pattern. Inflammatory processes are represented by widening of the folds, or by their complete absence. In tuberculosis, the mucosal pattern is nodular and stiff and the motility is abnormal. In cases of gastric or jejunal ulcer, the folds of the jejunum are commonly widened and the passage of the barium is rapid. Ascarides produce typical narrow, band-like shadows of diminished density within the lumen of the intestine, due to displacement of the contrast material.

In the diagnosis of stenosis and stricture, one has to keep in mind that the small intestines rapidly change their positions and a localization can be accomplished only with the aid of careful following of the passage of the contrast material. In the early stages of stenosis one occasionally sees transitory enlargement of the loops but no delay in emptying, or, more rarely, stenotic peristalses. If the stenosis is fully developed, the signs of ileus are present, consisting of air bubbles, fluid levels and dilated loops. The Kerkring's folds become so widely separated that they may be mistaken for colonic haustra. Lead poisoning, tetany and tuberculous peritonitis may produce similar changes. The clinical picture is the deciding factor in differentiation. Small intestinal loops may become dilated in cases of large intestinal stenosis also. Barium enema may be necessary for localization.

Tumors of the small intestines are rare and occur only in 2 to 3 per cent of cases of all intestinal tumors. The signs consist of localized narrowing of the lumen with smooth contours. Tumors of the ileocecal region may lead to an invagination of the ileum into the cecum. —*Eugene Freedman.*

RUTLEDGE, C. P. The diagnosis of diverticulitis and diverticulosis of the colon. *South. M. J.*, April, 1935, *28*, 303–308.

The conditions are discussed in general and the roentgen examination, both by the opaque meal and by the opaque enema, is evaluated. In the majority of cases the combined study gives the most information. The opaque meal is contraindicated in the acute or obstructive cases. In the presence of spasticity and marked localized tenderness, rest in bed with restriction of diet to liquids and re-examination will frequently permit a definite diagnosis.—*W. R. Brooksher.*

REEVES, ROBERT J., and HARRISON, EDWARD K. The treatment of hypotonic megacolon by administration of pancreatic tissue extract. *Radiology*, June, 1937, *28*, 731–735.

The authors have had some good results in treating Hirschsprung's disease and hypotonic colons with subcutaneous injections of pancreatic tissue extract. They used the extract No. 568 prepared by Sharp and Dohme in collaboration with Dr. Joseph Wolfe. Dosage varied from 1–5 cc. depending upon the severity of the condition. The action of this extract is that of epinephrine antagonist, stimulating the parasympathetics and producing a more normal rhythm of the intestine.—*J. H. Harris.*

PAUL, L. W. The roentgen diagnosis of carcinoma of the pancreas. *Am. J. Cancer*, Dec., 1936, *28*, 720–734.

The author presents 23 cases of proved carcinoma of the pancreas, each one of which had been examined roentgenologically by means of barium meal. In 3 cases, the roentgen examination was reported negative and later proved incorrect; in 8 cases, the diagnosis of a mass in the pancreas was later proved correct; in the remaining cases, there were abnormal findings which were misinterpreted or concerning which no definite conclusions were drawn, although later proved to have carcinoma of the pancreas. Carcinoma of the pancreas in 2 cases produced downward displacement of the duodenal bulb and pylorus, and in others it frequently failed to produce the classical sign of the enlargement of the duodenal curve. The problem of differential diagnosis, along with the difficulty of demonstrating a mass in the area, caused the author to conclude that reports of carcinoma of the pancreas should be made conservatively. A review of the scanty literature and 9 plates are included.—*J. S. Weber.*

HILL, HAROLD A. Functional disorders of the extra-hepatic biliary system: biliary dyssynergia or dyskinesia. *Radiology*, Sept., 1937, *29*, 261–278.

The extensive literature concerning the physiology of the intrabiliary tract is reviewed by the author. The three important facts upon which the discharge of bile depends are the secretory pressure of the liver, the contractility of the gallbladder and the sphincteric action of the intramural portion of the common bile duct. He concludes from the evidence available to date, that it seems that functional disorders of the extrahepatic biliary tract are relatively rare, especially if those due to associated organic lesions are excluded. The physiological disturbances that can be diagnosed are the hypertonic and atonic types of motor disorders, the former more frequent and is usually exhibited as a spasticity of the sphincteric mechanism. The symptoms of the spastic disorders are similar to those of a case of mild gallstone colic, while a case of gastrointestinal dyspepsia is simulated in the atonic form by dysfunctioning.

The diagnosis depends upon careful correlation of the findings of the history, duodenal intubation and roentgenological studies. The most significant cholecystographic evidence is found only if serial studies are made following ingestion of the fatty meal. An extensive bibliography is included.—*J. H. Harris.*

Rhodes, Robert L., and Greenblatt, Robert B. Carcinoma of the gallbladder: studies of 24 cases in Georgia. *South. M. J.*, March, 1937, *30*, 315–318.

The authors analyze 24 cases of carcinoma of the gallbladder admitted to the University Hospital of the Georgia School of Medicine. Jaundice was present in 13 cases while pain occurred in 18, 12 of which were proved to have calculi. Pain dated back longer than any other symptom and became progressively worse, being the chief factor in sending the patient to the physician. While bile was found in the urine of 8 patients, all of whom had jaundice, 5 patients with jaundice did not show bile in the urine. The usual complaint of "indigestion" was noted in only 12. But one complained of itching at the time of admission. Eleven had lost weight; an extensive invasion being found in 3 who had lost as much as 50 pounds. A palpable tumor was found in 13; of these 7 had palpable tumor and liver, 5 had palpable liver but not tumor, 18 had either palpable tumor or liver. Bleeding time was increased in but one case. Cholecystographic studies in 15 patients showed no dye in 9 cases. In only 7 was cancer of the gallbladder or pancreas suspected; the remainder were diagnosed gallbladder disease except one that was thought to be peptic ulcer. All patients have died, only one surviving as long as five years. —*W. R. Brooksher.*

Martin, Charles L. Roentgen ray studies of cirrhosis of the liver. *Texas State J. Med.*, Dec., 1936, *32*, 527–529.

Changes in the liver and spleen in hepatic cirrhosis can be roentgenologically demonstrated by thorium dioxide and by the use of pneumoperitoneun. No sequelae follow the latter procedure, which outlines the liver and spleen almost completely and permits detection of adhesions and accurate measurement. The findings in 10 cases are detailed.—*W. R. Brooksher.*

Yater, Wallace M., and Cavanagh, John R. The diagnosis of solitary liver abscess by means of thorotrast hepatosplenography. *Ann. Int. Med.*, August, 1937, *11*, 404–409.

Detailed report is made of a case of solitary liver abscess followed through to recovery by hepatosplenograms. Differentiation is to be made from neoplasms and cysts, the former, especially metastatic carcinoma, are usually multiple and appear as rounded areas of decreased opacity with a clearcut edge and often a surrounding halo of condensed liver tissue. Solitary liver tumors are rare but have a sharper outline than abscess, as does echinococcus cyst. The outline of an abscess is irregularly circular, hazy, and blends with the adjacent liver tissue. The central portion presents a homogeneous appearance. Considered with the clinical history, the roentgenogram should be pathognomonic.—*W. R. Brooksher.*

Berman, Theodore M. Miliary calcifications in the spleen. *Radiology*, July, 1937, *29*, 37–39.

A brief survey of the literature regarding the etiology of miliary calcification in the spleen is given. The author reports the finding in 18 cases showing such opacities in the spleen. Histological studies were made of these cases. The presence of calcified tuberculosis in the lungs does not warrant the assumption that the calcifications in the spleen are tuberculous. The conclusion is made that the majority of these miliary opacities represent phleboliths.—*J. H. Harris.*

GYNECOLOGY AND OBSTETRICS

JACOBS, J. BAY. Roentgenography in obstetrics. *Radiology*, April, 1937, *28*, 406–426.

The author summarizes nine methods of pelvimetry, giving the advantage and limitation of each. He goes into considerable detail in describing his method of measuring the pelvis. Those interested must read the article as such detail of technique cannot be abstracted satisfactorily. He concludes that the amount of roentgen exposure for the diagnostic procedures has been found to be free of danger to either the mother or child. The lateral view of the pelvis is of great value in these measurements. However, in the last analysis, the information gained by roentgenographic study should not supersede the clinical judgment of the attending obstetrician.—*J. H. Harris.*

PEACOCK. ALEXANDER H. Calcified fibromyoma of the uterus simulating large vesical calculus. *Northwest Med.*, Dec., 1936, *35*, 456–459.

Report is made of a case of calcified fibromyoma of the uterus, the uterine lesion being originally unsuspected. A urologic study with the cystogram determined the true condition. —*W. R. Brooksher.*

GENITOURINARY SYSTEM

SENGER, FEDOR L., and RUGGIERO, A. A comparative study of intravenous and subcutaneous urography. *Med. Times*, August, 1936, *64*, 275–278.

Description is given of the injection of the dye for excretory urography by clysis, using a 10 per cent solution into the axillae. The method is useful where one is unable to employ the intravenous route or retrograde urography. No reactions or complaints followed its use in 50 cases. Excretion is, of course, slower than by the intravenous route. The minor and major calyces were better demonstrated by this procedure while the ureter was best shown by the intravenous method.—*W. R. Brooksher.*

BURGENER, A. Das Pyelogramm bei Nierentumoren. (The pyelogram in tumors of the kidney.) *Röntgenpraxis*, Feb., 1937, *9*, 98–110.

In the differential diagnosis of tumors of the kidney, pyelography is of great importance. It allows the early diagnosis and differentiation between extrarenal, renal and retroperitoneal tumors.

The differential diagnosis between the various types of malignant tumors (hypernephromas, malignant nephromas, sarcomas and carcinomas) is impossible.

According to Carman and Braasch, the following pyelographic changes are found in kidney tumors: elongation of one or more calyces or of the true pelvis; narrowing of the individual calyces or obliteration of one or more calyces; broadening of calyces; pyelectasia and deformities of the kidney pelves.

The author reviewed the roentgen findings in 21 kidney tumors seen between 1923 and 1935 at the Surgical Clinic of the University of Zurich. He has grouped his cases according to the deformities they produce on the various parts of the kidney: the pelves, calyces and upper ureters. He calls attention to the changes in the size of the kidney as seen on the flat film, and also to the widening of the parenchymatous substance as seen on the pyelograms. He found that the distance between the contour of the contrast material containing kidney pelvis and the outer contour of the kidney shadow measured over 4 cm. in the majority of tumor cases. In one case, areas of calcification in the central portion of the kidney tumor were seen.

The author concludes that the pyelographic changes caused by malignant tumors are characteristic and allow the establishment of an unequivocal diagnosis. The tumors produce various changes in the pyelograms, none of which are conclusive by themselves. The diagnosis is made by finding a combination of several of these.—*Eugene Freedman.*